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(54) Title: 5' ESTS AND ENCODED HUMAN PROTEINS

(57) Abstract

The sequences of 5' ESTs derived from mRNAs encoding secreted proteins are disclosed. The 5' ESTs may be to obtain cDNAs and genomic DNAs corresponding to the 5' ESTs. The 5' ESTs may also be used in diagnostic, forensic, gene therapy, and chromosome mapping procedures. Upstream regulatory sequences may also be otained using the 5' ESTs. The 5' ESTs may also be used to design expression vectors and secretion vectors.

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5' ESTS AND ENCODED HUMAN PROTEINS

Background of the Invention

The estimated 50,000-100,000 genes scattered along the human chromosomes offer tremendous promise for the understanding, diagnosis, and treatment of human diseases. In addition, probes capable of specifically hybridizing to loci distributed throughout the human genome find applications in the construction of high resolution chromosome maps and in the identification of individuals.

In the past, the characterization of even a single human gene was a painstaking process, requiring years of effort. Recent developments in the areas of cloning vectors, DNA sequencing, and computer technology have merged to greatly accelerate the rate at which human genes can be isolated, sequenced, mapped, and characterized.

Currently, two different approaches are being pursued for identifying and characterizing the genes distributed along the human genome. In one approach, large fragments of genomic DNA are isolated, cloned, and sequenced. Potential open reading frames in these genomic sequences are identified using bioinformatics software. However, this approach entails sequencing large stretches of human DNA which do not encode proteins in order to find the protein encoding sequences scattered throughout the genome. In addition to requiring extensive sequencing, the bioinformatics software may mischaracterize the genomic sequences obtained, *i.e.*, labeling non-coding DNA as coding DNA and vice versa.

An alternative approach takes a more direct route to identifying and characterizing human genes. In this approach, complementary DNAs (cDNAs) are synthesized from isolated messenger RNAs (mRNAs) which encode human proteins. Using this approach, sequencing is only performed on DNA which is derived from protein coding portions of the genome. Often, only short stretches of the cDNAs are sequenced to obtain sequences called expressed sequence tags (ESTs). The ESTs may then be used to isolate or purify extended cDNAs which include sequences adjacent to the EST sequences. The extended cDNAs may contain all of the sequence of the EST which was used to obtain them or only a portion of the sequence of the EST which was used to obtain them. In addition, the extended cDNAs may contain the full coding sequence of the gene from which the EST was derived or, alternatively, the extended cDNAs may include portions of the coding sequence of the gene from which the EST was derived. It will be appreciated that there may be several extended cDNAs which include the EST sequence as a result of alternate splicing or the activity of alternative promoters. Alternatively, ESTs having partially overlapping sequences may be identified and contigs comprising the consensus sequences of the overlapping ESTs may be identified.

In the past, these short EST sequences were often obtained from oligo-dT primed cDNA

35 libraries. Accordingly, they mainly corresponded to the 3' untranslated region of the mRNA. In part, the prevalence of EST sequences derived from the 3' end of the mRNA is a result of the fact that typical

techniques for obtaining cDNAs, are not well suited for isolating cDNA sequences derived from the 5' ends of mRNAs (Adams et al., Nature 377:3-174, 1996, Hillier et al., Genome Res. 6:807-828, 1996).

In addition, in those reported instances where longer cDNA sequences have been obtained, the reported sequences typically correspond to coding sequences and do not include the full 5' untranslated 5 region (5'UTR) of the mRNA from which the cDNA is derived. Indeed, 5'UTRs have been shown to affect either the stability or translation of mRNAs. Thus, regulation of gene expression may be achieved through the use of alternative 5'UTRs as shown, for instance, for the translation of the tissue inhibitor of metalloprotease mRNA in mitogenically activated cells (Waterhouse et al, J Biol Chem. 265:5585-9. 1990). Furthermore, modification of 5'UTR through mutation, insertion or translocation events 10 may even be implied in pathogenesis. For instance, the fragile X syndrome, the most common cause of inherited mental retardation, is partly due to an insertion of multiple CGG trinucleotides in the 5'UTR of the fragile X mRNA resulting in the inhibition of protein synthesis via ribosome stalling (Feng et al, Science 268:731-4, 1995). An aberrant mutation in regions of the 5'UTR known to inhibit translation of the proto-oncogene c-myc was shown to result in upregulation of c-myc protein 15 levels in cells derived from patients with multiple myelomas (Willis et al, Curr Top Microbiol Immunol 224:269-76, 1997). In addition, the use of oligo-dT primed cDNA libraries does not allow the isolation of complete 5'UTRs since such incomplete sequences obtained by this process may not include the first exon of the mRNA, particularly in situations where the first exon is short. Furthermore, they may not include some exons, often short ones, which are located upstream of splicing sites. Thus, there 20 is a need to obtain sequences derived from the 5' ends of mRNAs.

While many sequences derived from human chromosomes have practical applications, approaches based on the identification and characterization of those chromosomal sequences which encode a protein product are particularly relevant to diagnostic and therapeutic uses. In some instances, the sequences used in such therapeutic or diagnostic techniques may be sequences which encode proteins which are secreted from the cell in which they are synthesized. Those sequences encoding secreted proteins as well as the secreted proteins themselves, are particularly valuable as potential therapeutic agents. Such proteins are often involved in cell to cell communication and may be responsible for producing a clinically relevant response in their target cells. In fact, several secretory proteins, including tissue plasminogen activator, G-CSF, GM-CSF, erythropoietin, human growth hormone, insulin, interferon-α, interferon-β, interferon-γ, and interleukin-2, are currently in clinical use. These proteins are used to treat a wide range of conditions, including acute myocardial infarction, acute ischemic stroke, anemia, diabetes, growth hormone deficiency, hepatitis, kidney carcinoma, chemotherapy-induced neutropenia and multiple sclerosis. For these reasons, extended cDNAs encoding secreted proteins or portions thereof represent a valuable source of therapeutic agents. Thus, there is a need for the identification and characterization of secreted proteins and the nucleic acids encoding them.

In addition to being therapeutically useful themselves, secretory proteins include short peptides, called signal peptides, at their amino termini which direct their secretion. These signal peptides are

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encoded by the signal sequences located at the 5' ends of the coding sequences of genes encoding secreted proteins. These signal peptides can be used to direct the extracellular secretion of any protein to which they are operably linked. In addition, portions of the signal peptides called membranetranslocating sequences, may also be used to direct the intracellular import of a peptide or protein of 5 interest. This may prove beneficial in gene therapy strategies in which it is desired to deliver a particular gene product to cells other than the cells in which it is produced. Signal sequences encoding signal peptides also find application in simplifying protein purification techniques. In such applications, the extracellular secretion of the desired protein greatly facilitates purification by reducing the number of undesired proteins from which the desired protein must be selected. Thus, there exists a need to identify 10 and characterize the 5' portions of the genes for secretory proteins which encode signal peptides.

Sequences coding for non-secreted proteins may also find application as therapeutics or diagnostics. In particular, such sequences may be used to determine whether an individual is likely to express a detectable phenotype, such as a disease, as a consequence of a mutation in the coding sequence of a protein. In instances where the individual is at risk of suffering from a disease or other undesirable 15 phenotype as a result of a mutation in such a coding sequence, the undesirable phenotype may be corrected by introducing a normal coding sequence using gene therapy. Alternatively, if the undesirable phenotype results from overexpression of the protein encoded by the coding sequence, expression of the protein may be reduced using antisense or triple helix based strategies.

The secreted or non-secreted human polypeptides encoded by the coding sequences may also be 20 used as therapeutics by administering them directly to an individual having a condition, such as a disease, resulting from a mutation in the sequence encoding the polypeptide. In such an instance, the condition can be cured or ameliorated by administering the polypeptide to the individual.

In addition, the secreted or non-secreted human polypeptides or portions thereof may be used to generate antibodies useful in determining the tissue type or species of origin of a biological sample. The 25 antibodies may also be used to determine the cellular localization of the secreted or non-secreted human polypeptides or the cellular localization of polypeptides which have been fused to the human polypeptides. In addition, the antibodies may also be used in immunoaffinity chromatography techniques to isolate, purify, or enrich the human polypeptide or a target polypeptide which has been fused to the human polypeptide.

Public information on the number of human genes for which the promoters and upstream regulatory regions have been identified and characterized is quite limited. In part, this may be due to the difficulty of isolating such regulatory sequences. Upstream regulatory sequences such as transcription factor binding sites are typically too short to be utilized as probes for isolating promoters from human genomic libraries. Recently, some approaches have been developed to isolate human promoters. One of 35 them consists of making a CpG island library (Cross et al., Nature Genetics 6: 236-244, 1994). The second consists of isolating human genomic DNA sequences containing SpeI binding sites by the use of Spel binding protein. (Mortlock et al., Genome Res. 6:327-335, 1996). Both of these approaches have

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their limits due to a lack of specificity and of comprehensiveness. Thus, there exists a need to identify and systematically characterize the 5' portions of the genes.

The present 5' ESTs may be used to efficiently identify and isolate 5'UTRs and upstream regulatory regions which control the location, developmental stage, rate, and quantity of protein synthesis, as well as the stability of the mRNA. Once identified and characterized, these regulatory regions may be utilized in gene therapy or protein purification schemes to obtain the desired amount and locations of protein synthesis or to inhibit, reduce, or prevent the synthesis of undesirable gene products.

In addition, ESTs containing the 5' ends of protein genes may include sequences useful as probes for chromosome mapping and the identification of individuals. Thus, there is a need to identify and characterize the sequences upstream of the 5' coding sequences of genes.

Summary of the Invention

The present invention relates to purified, isolated, or enriched 5' ESTs which include sequences derived from the authentic 5' ends of their corresponding mRNAs. The term "corresponding mRNA"

15 refers to the mRNA which was the template for the cDNA synthesis which produced the 5' EST. These sequences will be referred to hereinafter as "5' ESTs." The present invention also includes purified, isolated or enriched nucleic acids comprising contigs assembled by determining a consensus sequences from a plurality of ESTs containing overlapping sequences. These contigs will be referred to herein as "consensus contigated 5'ESTs."

As used herein, the term "purified" does not require absolute purity; rather, it is intended as a relative definition. Individual 5' EST clones isolated from a cDNA library have been conventionally purified to electrophoretic homogeneity. The sequences obtained from these clones could not be obtained directly either from the library or from total human DNA. The cDNA clones are not naturally occurring as such, but rather are obtained via manipulation of a partially purified naturally occurring substance (messenger RNA). The conversion of mRNA into a cDNA library involves the creation of a synthetic substance (cDNA) and pure individual cDNA clones can be isolated from the synthetic library by clonal selection. Thus, creating a cDNA library from messenger RNA and subsequently isolating individual clones from that library results in an approximately 10⁴-10⁶ fold purification of the native message. Purification of starting material or natural material to at least one order of magnitude,

preferably two or three orders, and more preferably four or five orders of magnitude is expressly contemplated.

As used herein, the term "isolated" requires that the material be removed from its original environment (e.g., the natural environment if it is naturally occurring). For example, a naturally-occurring polynucleotide present in a living animal is not isolated, but the same polynucleotide, separated from some or all of the coexisting materials in the natural system, is isolated.

As used herein, the term "recombinant" means that the 5' EST is adjacent to "backbone" nucleic acid to which it is not adjacent in its natural environment. Additionally, to be "enriched" the 5' ESTs will

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represent 5% or more of the number of nucleic acid inserts in a population of nucleic acid backbone molecules. Backbone molecules according to the present invention include nucleic acids such as expression vectors, self-replicating nucleic acids, viruses, integrating nucleic acids, and other vectors or nucleic acids used to maintain or manipulate a nucleic acid insert of interest. Preferably, the enriched 5' ESTs represent 15% or more of the number of nucleic acid inserts in the population of recombinant backbone molecules. More preferably, the enriched 5' ESTs represent 50% or more of the number of nucleic acid inserts in the population of recombinant backbone molecules. In a highly preferred embodiment, the enriched 5' ESTs represent 90% or more of the number of nucleic acid inserts in the population of recombinant backbone molecules.

"Stringent," "moderate," and "low" hybridization conditions are as defined below.

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The term "polypeptide" refers to a polymer of amino acids without regard to the length of the polymer; thus, peptides, oligopeptides, and proteins are included within the definition of polypeptide. This term also does not specify or exclude post-expression modifications of polypeptides, for example, polypeptides which include the covalent attachment of glycosyl groups, acetyl groups, phosphate groups, lipid groups and the like are expressly encompassed by the term polypeptide. Also included within the definition are polypeptides which contain one or more analogs of an amino acid (including, for example, non-naturally occurring amino acids, amino acids which only occur naturally in an unrelated biological system, modified amino acids from mammalian systems etc.), polypeptides with substituted linkages, as well as other modifications known in the art, both naturally occurring and non-naturally occurring.

As used interchangeably herein, the terms "nucleic acids," "oligonucleotides," and "polynucleotides" include RNA, DNA, or RNA/DNA hybrid sequences of more than one nucleotide in either single chain or duplex form. The term "nucleotide" as used herein as an adjective to describe molecules comprising RNA, DNA, or RNA/DNA hybrid sequences of any length in single-stranded or duplex form. The term "nucleotide" is also used herein as a noun to refer to individual nucleotides or varieties of nucleotides, meaning a molecule, or individual unit in a larger nucleic acid molecule, comprising a purine or pyrimidine, a ribose or deoxyribose sugar moiety, and a phosphate group, or phosphodiester linkage in the case of nucleotides within an oligonucleotide or polynucleotide. Although the term "nucleotide" is also used herein to encompass "modified nucleotides" which comprise at least one modifications (a) an alternative linking group, (b) an analogous form of purine, (c) an analogous form of pyrimidine, or (d) an analogous sugar, for examples of analogous linking groups, purine, pyrimidines, and sugars see for example PCT publication No. WO 95/04064. The polynucleotide sequences of the invention may be prepared by any known method, including synthetic, recombinant, ex vivo generation, or a combination thereof, as well as utilizing any purification methods known in the art.

The terms "base paired" and "Watson & Crick base paired" are used interchangeably herein to refer to nucleotides which can be hydrogen bonded to one another be virtue of their sequence

identities in a manner like that found in double-helical DNA with thymine or uracil residues linked to adenine residues by two hydrogen bonds and cytosine and guanine residues linked by three hydrogen bonds (See Stryer, L., Biochemistry, 4th edition, 1995).

The terms "complementary" or "complement thereof" are used herein to refer to the 5 sequences of polynucleotides which are capable of forming Watson & Crick base pairing with another specified polynucleotide throughout the entirety of the complementary region. For the purpose of the present invention, a first polynucleotide is deemed to be complementary to a second polynucleotide when each base in the first polynucleotide is paired with its complementary base. Complementary bases are, generally, A and T (or A' and U), or C and G. "Complement" is used 10 herein as a synonym from "complementary polynucleotide," "complementary nucleic acid" and "complementary nucleotide sequence". These terms are applied to pairs of polynucleotides based solely upon their sequences and not any particular set of conditions under which the two polynucleotides would actually bind. Preferably, a "complementary" sequence is a sequence which an A at each position where there is a T on the opposite strand, a T at each position where there is an A on 15 the opposite strand, a G at each position where there is a C on the opposite strand and a C at each position where there is a G on the opposite strand.

Thus, 5' ESTs in cDNA libraries in which one or more 5' ESTs make up 5% or more of the number of nucleic acid inserts in the backbone molecules are "enriched recombinant 5' ESTs" as defined herein. Likewise, 5' ESTs in a population of plasmids in which one or more 5' ESTs of the present 20 invention have been inserted such that they represent 5% or more of the number of inserts in the plasmid backbone are "enriched recombinant 5' ESTs" as defined herein. However, 5' ESTs in cDNA libraries in which 5' ESTs constitute less than 5% of the number of nucleic acid inserts in the population of backbone molecules, such as libraries in which backbone molecules having a 5' EST insert are extremely rare, are not "enriched recombinant 5' ESTs."

In some embodiments, the present invention relates to 5' ESTs which are derived from genes encoding secreted proteins. As used herein, a "secreted" protein is one which, when expressed in a suitable host cell, is transported across or through a membrane, including transport as a result of signal peptides in its amino acid sequence. "Secreted" proteins include without limitation proteins secreted wholly (e.g. soluble proteins), or partially (e.g. receptors) from the cell in which they are expressed. 30 "Secreted" proteins also include without limitation proteins which are transported across the membrane of the endoplasmic reticulum.

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Such 5' ESTs include nucleic acid sequences, called signal sequences, which encode signal peptides which direct the extracellular secretion of the proteins encoded by the genes from which the 5' ESTs are derived. Generally, the signal peptides are located at the amino termini of secreted proteins.

Secreted proteins are translated by ribosomes associated with the "rough" endoplasmic reticulum. Generally, secreted proteins are co-translationally transferred to the membrane of the endoplasmic reticulum. Association of the ribosome with the endoplasmic reticulum during translation

of secreted proteins is mediated by the signal peptide. The signal peptide is typically cleaved following its co-translational entry into the endoplasmic reticulum. After delivery to the endoplasmic reticulum, secreted proteins may proceed through the Golgi apparatus. In the Golgi apparatus, the proteins may undergo post-translational modification before entering secretory vesicles which transport them across 5 the cell membrane.

The 5' ESTs of the present invention have several important applications. For example, they may be used to obtain and express cDNA clones which include the full protein coding sequences of the corresponding gene products, including the authentic translation start sites derived from the 5' ends of the coding sequences of the mRNAs from which the 5' ESTs are derived. These cDNAs will be referred 10 to hereinafter as "full-length cDNAs." These cDNAs may also include DNA derived from mRNA sequences upstream of the translation start site. The full-length cDNA sequences may be used to express the proteins corresponding to the 5' ESTs. As discussed above, secreted proteins and non-secreted proteins may be therapeutically important. Thus, the proteins expressed from the cDNAs may be useful in treating and controlling a variety of human conditions. The 5' ESTs may also be used to obtain the 15 corresponding genomic DNA. The term "corresponding genomic DNA" refers to the genomic DNA which encodes the mRNA from which the 5' EST was derived.

Alternatively, the 5' ESTs may be used to obtain and express extended cDNAs encoding portions of the protein. In the case of secreted proteins, the portions may comprise the signal peptides of the secreted proteins or the mature proteins generated when the signal peptide is cleaved off.

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The present invention includes isolated, purified, or enriched "EST-related nucleic acids." The terms "isolated," "purified" or "enriched" have the meanings provided above. As used herein, the term "EST-related nucleic acids" means the nucleic acids of SEQ ID NOs. 24-811 and 1600-1622, extended cDNAs obtainable using the nucleic acids of SEQ ID NOs. 24-811 and 1600-1622, full-length cDNAs obtainable using the nucleic acids of SEQ ID NOs. 24-811 and 1600-1622 or genomic DNAs obtainable 25 using the nucleic acids of SEQ ID NOs. 24-811 and 1600-1622. The present invention also includes the sequences complementary to the EST-related nucleic acids.

The present invention also includes isolated, purified, or enriched "fragments of EST-related nucleic acids." The terms "isolated," "purified" and "enriched" have the meanings described above. As used herein the term "fragments of EST-related nucleic acids" means fragments comprising at least 10, 30 12, 15, 18, 20, 23, 25, 28, 30, 35, 40, 50, 75, 100, 200, 300, 500, or 1000 consecutive nucleotides of the EST-related nucleic acids to the extent that fragments of these lengths are consistent with the lengths of the particular EST-related nucleic acids being referenced. In particular, fragments of EST-related nucleic acids refer to "polynucleotides described in Table II," "polynucleotides described in Table III," and "polynucleotides described in Table IV." The present invention also includes the sequences 35 complementary to the fragments of the EST-related nucleic acids.

The present invention also includes isolated, purified, or enriched "positional segments of ESTrelated nucleic acids." As used herein, the term "positional segments of EST-related nucleic acids"

includes segments comprising nucleotides 1-25, 26-50, 51-75, 76-100, 101-125, 126-150, 151-175, 176-200, 201-225, 226-250, 251-300, 301-325, 326-350, 351-375, 376-400, 401-425, 426-450, 451-475, 476-500, 501-525, 526-550, 551-575, 576-600 and 601-the terminal nucleotide of the EST-related nucleic acids to the extent that such nucleotide positions are consistent with the lengths of the particular 5 EST-related nucleic acids being referenced. The term "positional segments of EST-related nucleic acids also includes segments comprising nucleotides 1-50, 51-100, 101-150, 151-200, 201-250, 251-300, 301-350, 351-400, 401-450, 450-500, 501-550, 551-600 or 601-the terminal nucleotide of the EST-related nucleic acids to the extent that such nucleotide positions are consistent with the lengths of the particular EST-related nucleic acids being referenced. The term "positional segments of EST-related nucleic 10 acids" also includes segments comprising nucleotides 1-100, 101-200, 201-300, 301-400, 501-500, 500-600, or 601-the terminal nucleotide of the EST-related nucleic acids to the extent that such nucleotide positions are consistent with the lengths of the particular EST-related nucleic acids being referenced. In addition, the term "positional segments of EST-related nucleic acids" includes segments comprising nucleotides 1-200, 201-400, 400-600, or 601-the terminal nucleotide of the EST-related nucleic acids to 15 the extent that such nucleotide positions are consistent with the lengths of the particular EST-related nucleic acids being referenced. The present invention also includes the sequences complementary to the positional segments of EST-related nucleic acids.

The present invention also includes isolated, purified, or enriched "fragments of positional segments of EST-related nucleic acids." As used herein, the term "fragments of positional segments of EST-related nucleic acids" refers to fragments comprising at least 10, 15, 18, 20, 23, 25, 28, 30, 35, 40, 50, 75, 100, 150, or 200 consecutive nucleotides of the positional segments of EST-related nucleic acids. The present invention also includes the sequences complementary to the fragments of positional segments of EST-related nucleic acids.

The present invention also includes isolated or purified "EST-related polypeptides." As used

berein, the term "EST-related polypeptides" means the polypeptides encoded by the EST-related nucleic acids, including the polypeptides of SEQ ID NOs. 812-1599.

The present invention also includes isolated or purified "fragments of EST-related polypeptides." As used herein, the term "fragments of EST-related polypeptides" means fragments comprising at least 5, 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, or 150 consecutive amino acids of an EST-related polypeptide to the extent that fragments of these lengths are consistent with the lengths of the particular EST-related polypeptides being referenced. In particular, fragments of EST-related polypeptides refer to polypeptides encoded by "polynucleotides described in Table II," "polynucleotides described in Table III," and "polynucleotides described in Table IV."

The present invention also includes isolated or purified "positional segments of EST-related polypeptides." As used herein, the term "positional segments of EST-related polypeptides" includes polypeptides comprising amino acid residues 1-25, 26-50, 51-75, 76-100, 101-125, 126-150, 151-175, 176-200, or 201-the C-terminal amino acid of the EST-related polypeptides to the extent that such amino

acid residues are consistent with the lengths of the particular EST-related polypeptides being referenced. The term "positional segments of EST-related polypeptides also includes segments comprising amino acid residues 1-50, 51-100, 101-150, 151-200 or 201-the C-terminal amino acid of the EST-related polypeptides to the extent that such amino acid residues are consistent with the lengths of the particular 5 EST-related polypeptides being referenced. The term "positional segments of EST-related polypeptides" also includes segments comprising amino acids 1-100 or 101-200 of the EST-related polypeptides to the extent that such amino acid residues are consistent with the lengths of particular EST-related polypeptides being referenced. In addition, the term "positional segments of EST-related polypeptides" includes segments comprising amino acid residues 1-200 or 201-the C-terminal amino acid of the EST-10 related polypeptides to the extent that amino acid residues are consistent with the lengths of the particular EST-related polypeptides being referenced.

The present invention also includes isolated or purified "fragments of positional segments of EST-related polypeptides." As used herein, the term "fragments of positional segments of EST-related polypeptides" means fragments comprising at least 5, 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, or 150 15 consecutive amino acids of positional segments of EST-related polypeptides to the extent that fragments of these lengths are consistent with the lengths of the particular EST-related polypeptides being referenced.

The present invention also includes antibodies which specifically recognize the EST-related polypeptides, fragments of EST-related polypeptides, positional segments of EST-related polypeptides, 20 or fragments of positional segments of EST-related polypeptides. In the case of secreted proteins, such as those of SEQ ID NOs. 1554-1580 antibodies which specifically recognize the mature protein generated when the signal peptide is cleaved may also be obtained as described below. Similarly, antibodies which specifically recognize the signal peptides of SEQ ID NOs. 812-1516 or 1554-1580 may also be obtained.

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In some embodiments and in the case of secreted proteins, the EST-related nucleic acids, fragments of EST-related nucleic acids, positional segments of EST-related nucleic acids, or fragments of positional segments of nucleic acids include a signal sequence. In other embodiments, the ESTrelated nucleic acids, fragments of EST-related nucleic acids, positional segments of EST-related nucleic acids, or fragments of positional segments of nucleic acids may include the full coding sequence for the 30 protein or, in the case of secreted proteins, the full coding sequence of the mature protein (i.e. the protein generated when the signal polypeptide is cleaved off). In addition, the EST-related nucleic acids, fragments of EST-related nucleic acids, positional segments of EST-related nucleic acids, or fragments of positional segments of nucleic acids may include regulatory regions upstream of the translation start site or downstream of the stop codon which control the amount, location, or developmental stage of gene 35 expression.

As discussed above, both secreted and non-secreted human proteins may be therapeutically important. Thus, the proteins expressed from the EST-related nucleic acids, fragments of EST-related nucleic acids, positional segments of EST-related nucleic acids, or fragments of positional segments of nucleic acids may be useful in treating or controlling a variety of human conditions.

The EST-related nucleic acids, fragments of EST-related nucleic acids, positional segments of EST-related nucleic acids, or fragments of positional segments of nucleic acids may be used in forensic procedures to identify individuals or in diagnostic procedures to identify individuals having genetic diseases resulting from abnormal gene expression. In addition, the EST-related nucleic acids, fragments of EST-related nucleic acids, positional segments of EST-related nucleic acids, or fragments of positional segments of nucleic acids are useful for constructing a high resolution map of the human chromosomes.

The present invention also relates to secretion vectors capable of directing the secretion of a . protein of interest. Such vectors may be used in gene therapy strategies in which it is desired to produce a gene product in one cell which is to be delivered to another location in the body. Secretion vectors may also facilitate the purification of desired proteins.

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The present invention also relates to expression vectors capable of directing the expression of an inserted gene in a desired spatial or temporal manner or at a desired level. Such vectors may include sequences upstream of the EST-related nucleic acids, fragments of EST-related nucleic acids, positional segments of EST-related nucleic acids, or fragments of positional segments of nucleic acids, such as promoters or upstream regulatory sequences.

The present invention also comprises fusion vectors for making chimeric polypeptides

comprising a first polypeptide and a second polypeptide. Such vectors are useful for determining the
cellular localization of the chimeric polypeptides or for isolating, purifying or enriching the chimeric
polypeptides.

The EST-related nucleic acids, fragments of EST-related nucleic acids, positional segments of EST-related nucleic acids, or fragments of positional segments of nucleic acids may also be used for gene therapy to control or treat genetic diseases. In the case of secreted proteins, signal peptides may be fused to heterologous proteins to direct their extracellular secretion.

Bacterial clones containing Bluescript plasmids having inserts containing the sequence of the non-aligned 5'ESTs, also referred to as singletons, and sequences of the 5'ESTs which were aligned to yield consensus contigated 5' ESTs are presently stored at 80°C in 4% (v/v) glycerol in the inventor's laboratories under internal designations. The non-aligned 5'ESTs are those which comprise a single EST from a single tissue in the listing of Table V. The inserts may be recovered from the stored materials by growing the appropriate clones on a suitable medium. The Bluescript DNA can then be isolated using plasmid isolation procedures familiar to those skilled in the art such as alkaline lysis minipreps or large scale alkaline lysis plasmid isolation procedures. If desired the plasmid DNA may be further enriched by centrifugation on a cesium chloride gradient, size exclusion chromatography, or anion exchange chromatography. The plasmid DNA obtained using these procedures may then be manipulated using standard cloning techniques familiar to those skilled in the art. Alternatively, a PCR

can be performed with primers designed at both ends of the inserted EST-related nucleic acids, fragments of EST-related nucleic acids, positional segments of EST-related nucleic acids, or fragments of positional segments of nucleic acids. The PCR product which corresponds to the EST-related nucleic acids, fragments of EST-related nucleic acids, positional segments of EST-related nucleic acids, or fragments of positional segments of nucleic acids can then be manipulated using standard cloning techniques familiar to those skilled in the art.

One embodiment of the present invention is a purified nucleic acid comprising a sequence selected from the group consisting of SEQ ID NOs. 24-811 and SEQ ID NOs. 1600-1622 and sequences complementary to the sequences of SEQ ID NOs. 24-811 and SEQ ID NOs. 1600-1622.

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Another embodiment of the present invention is a purified nucleic acid comprising at least 10, 12, 15, 18, 20, 23, 25, 28, 30, 35, 40, 50, 75, 100, 200, 300, 500, or 1000 consecutive nucleotides, to the extent that fragments of these lengths are consistent with the specific sequence, of a sequence selected from the group consisting of SEQ ID NOs. 24-811 and SEQ ID NOs. 1600-1622 and sequences complementary to the sequences of SEQ ID NOs. 24-811 and SEQ ID NOs. 1600-1622.

A further embodiment of the present invention is a purified nucleic acid comprising the coding sequence of a sequence selected from the group consisting of SEQ ID NOs. 24-811.

Yet another embodiment of the present invention is a purified nucleic acid comprising the full coding sequences of a sequence selected from the group consisting of SEQ ID NOs. 766-792 wherein the full coding sequence comprises the sequence encoding the signal peptide and the sequence encoding the mature protein.

Still another embodiment of the present invention is a purified nucleic acid comprising a contiguous span of a sequence selected from the group consisting of SEQ ID NOs. 766-792 which encodes the mature protein.

Another embodiment of the present invention is a purified nucleic acid comprising a contiguous span of a sequence selected from the group consisting of SEQ ID NOs. 24-728 and 766-792 which encodes the signal peptide.

Another embodiment of the present invention is a purified nucleic acid encoding a polypeptide comprising a sequence selected from the group consisting of the sequences of SEQ ID NOs. 812-1599.

Another embodiment of the present invention is a purified nucleic acid encoding a polypeptide comprising a sequence selected from the group consisting of the sequences of SEQ ID NOs. 1554-1580.

Another embodiment of the present invention is a purified nucleic acid encoding a polypeptide comprising a mature protein included in a sequence selected from the group consisting of the sequences of SEQ ID NOs. 1554-1580.

Another embodiment of the present invention is a purified nucleic acid encoding a polypeptide comprising a signal peptide included in a sequence selected from the group consisting of the sequences of SEQ ID NOs. 812-1516 and 1554-1580.

Another embodiment of the present invention is a purified nucleic acid at least 30, 35, 40, 50, 75, 100, 200, 300, 500 or 1000 nucleotides in length which hybridizes under stringent conditions to a sequence selected from the group consisting of SEQ ID NOs. 24-811 and SEQ ID NOs. 1600-1622 and sequences complementary to the sequences of SEQ ID NOs. 24-811 and SEQ ID NOs. 1600-1622.

Another embodiment of the present invention is a purified or isolated polypeptide comprising a sequence selected from the group consisting of the sequences of SEQ ID NOs. 812-1599.

Another embodiment of the present invention is a purified or isolated polypeptide comprising a sequence selected from the group consisting of SEQ ID NOs. 1554-1580.

Another embodiment of the present invention is a purified or isolated polypeptide comprising a mature protein of a polypeptide selected from the group consisting of SEQ ID NOs. 1554-1580.

Another embodiment of the present invention is a purified or isolated polypeptide comprising a signal peptide of a sequence selected from the group consisting of the polypeptides of SEQ ID NOs. 812-1516 and 1554-1580.

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Another embodiment of the present invention is a purified or isolated polypeptide comprising at least 12, 15, 18, 20, 23, 25, 28, 30, 35, 40, 50, 75, 100, 200, 300, 500, or 1000 consecutive amino acids, to the extent that fragments of these lengths are consistent with the specific sequence, of a sequence selected from the group consisting of the sequences of SEQ ID NOs. 812-1599.

Another embodiment of the present invention is a method of making a cDNA comprising the steps of contacting a collection of mRNA molecules from human cells with a primer comprising at least 12, 15, 18, 20, 23, 25, 28, 30, 35, 40, or 50 consecutive nucleotides of a sequence selected from the group consisting of the sequences complementary to SEQ ID NOs. 24-811 and SEQ ID NOs. 1600-1622, hybridizing said primer to an mRNA in said collection that encodes said protein reverse transcribing said hybridized primer to make a first cDNA strand from said mRNA, making a second cDNA strand complementary to said first cDNA strand and isolating the resulting cDNA encoding said protein comprising said first cDNA strand and said second cDNA strand.

Another embodiment of the present invention is a purified cDNA obtainable by the method of the preceding paragraph.

In one aspect of this embodiment, the cDNA encodes at least a portion of a human polypeptide.

Another embodiment of the present invention is a method of making a cDNA comprising the steps of obtaining a cDNA comprising a sequence selected from the group consisting of SEQ ID NOs. 24-811 and SEQ ID NOs. 1600-1622, contacting said cDNA with a detectable probe comprising at least 12, 15, 18, 20, 23, 25, 28, 30, 35, 40, or 50 consecutive nucleotides of a sequence

selected from the group consisting of SEQ ID NOs. 24-811 and SEQ ID NOs. 1600-1622 and the sequences complementary to SEQ ID NOs. 24-811 and SEQ ID NOs. 1600-1622 under conditions which permit said probe to hybridize to said cDNA, identifying a cDNA which hybridizes to said detectable probe, and isolating said cDNA which hybridizes to said probe.

Another embodiment of the present invention is a purified cDNA obtainable by the method of the preceding paragraph.

In one aspect of this embodiment, the cDNA encodes at least a portion of a human polypeptide.

Another embodiment of the present invention is a method of making a cDNA comprising the steps of contacting a collection of mRNA molecules from human cells with a first primer capable of hybridizing to the polyA tail of said mRNA, hybridizing said first primer to said polyA tail, reverse transcribing said mRNA to make a first cDNA strand, making a second cDNA strand complementary to said first cDNA strand using at least one primer comprising at least 12, 15, 18, 20, 23, 25, 28, 30, 35, 40, or 50 consecutive nucleotides of a sequence selected from the group consisting of SEQ ID NOs. 24-811 and SEQ ID NOs. 1600-1622, and isolating the resulting cDNA comprising said first cDNA strand and said second cDNA strand.

Another embodiment of the present invention is a purified cDNA obtainable by the method of the preceding paragraph.

In one aspect of this embodiment, said cDNA encodes at least a portion of a human 20 polypeptide.

In another aspect of the preceding method the second cDNA strand is made by contacting said first cDNA strand with a first pair of primers, said first pair of primers comprising a second primer comprising at least 12, 15, 18, 20, 23, 25, 28, 30, 35, 40, or 50 consecutive nucleotides of a sequence selected from the group consisting of SEQ ID NOs. 24-811 and SEQ ID NOs. 1600-1622 and a third primer having a sequence therein which is included within the sequence of said first primer, performing a first polymerase chain reaction with said first pair of primers to generate a first PCR product, contacting said first PCR product with a second pair of primers, said second pair of primers comprising a fourth primer, said fourth primer comprising at least 12, 15, 18, 20, 23, 25, 28, 30, 35, 40, or 50 consecutive nucleotides of said sequence selected from the group consisting of SEQ ID NOs. 24-811 and SEQ ID NOs. 1600-1622, and a fifth primer, wherein said fourth and fifth hybridize to sequences within said first PCR product, and performing a second polymerase chain reaction, thereby generating a second PCR product.

One aspect of this embodiment is a purified cDNA obtainable by the method of the preceding paragraph.

In another aspect of this embodiment, said cDNA encodes at least a portion of a human polypeptide.

Alternatively, the second cDNA strand may be made by contacting said first cDNA strand with a second primer comprising at least 12, 15, 18, 20, 23, 25, 28, 30, 35, 40, or 50 consecutive nucleotides of a sequence selected from the group consisting of SEQ ID NOs. 24-811 and SEQ ID NOs. 1600-1622, hybridizing said second primer to said first strand cDNA, and extending said by hybridized second primer to generate said second cDNA strand.

One aspect of the above embodiment is a purified cDNA obtainable by the method of the preceding paragraph.

In a further aspect of this embodiment said cDNA encodes at least a portion of a human polypeptide.

Another embodiment of the present invention is a method of making a polypeptide comprising the steps of obtaining a cDNA which encodes a polypeptide encoded by a nucleic acid comprising a sequence selected from the group consisting of SEQ ID NOs. 24-811 or a cDNA which encodes a polypeptide comprising at least 6, 8, 10, 12, 15, 18, 20, 23, 25, 28, 30, 35, 40, or 50 consecutive amino acids of a polypeptide encoded by a sequence selected from the group consisting of SEQ ID NOs. 24-811, inserting said cDNA in an expression vector such that said cDNA is operably linked to a promoter, introducing said expression vector into a host cell whereby said host cell produces the protein encoded by said cDNA, and isolating said protein.

Another aspect of this embodiment is an isolated protein obtainable by the method of the preceding paragraph.

Another embodiment of the present invention is a method of obtaining a promoter DNA comprising the steps of obtaining genomic DNA located upstream of a nucleic acid comprising a sequence selected from the group consisting of SEQ ID NOs. 24-811 and SEQ ID NOs. 1600-1622 and the sequences complementary to the sequences of SEQ ID NOs. 24-811 and SEQ ID NOs. 1600-1622, screening said genomic DNA to identify a promoter capable of directing transcription initiation, and isolating said DNA comprising said identified promoter.

In one aspect of this embodiment, said obtaining step comprises walking from genomic DNA comprising a sequence selected from the group consisting of SEQ ID NOs. 24-811 and SEQ ID NOs. 1600-1622 and the sequences complementary to SEQ ID NOs. 24-811 and SEQ ID NOs. 1600-1622. In another aspect of this embodiment, said screening step comprises inserting genomic DNA located upstream of a sequence selected from the group consisting of SEQ ID NOs. 24-811 and SEQ ID NOs. 1600-1622 and the sequences complementary to SEQ ID NOs. 24-811 and SEQ ID NOs. 1600-1622 into a promoter reporter vector. For example, said screening step may comprise identifying motifs in genomic DNA located upstream of a sequence selected from the group consisting of SEQ ID NOs. 24-811 and SEQ ID NOs. 1600-1622 and the sequences complementary to SEQ ID NOs. 24-811 and SEQ ID NOs. 1600-1622 which are transcription factor binding sites or transcription start sites.

Another embodiment of the present invention is a isolated promoter obtainable by the method of the paragraph above.

Another embodiment of the present invention is the inclusion of at least one sequence selected from the group consisting of SEQ ID NOs. 24-811 and SEQ ID NOs. 1600-1622, the sequences complementary to the sequences of SEQ ID NOs. 24-811 and SEQ ID NOs. 1600-1622 and fragments comprising at least 12, 15, 18, 20, 23, 25, 28, 30, 35, 40, 50, or 100 consecutive nucleotides of said sequence in an array of discrete ESTs or fragments thereof of at least 12, 15, 18, 20, 23, 25, 28, 30, 35, 40, 50, or 100 nucleotides in length. In some aspects of this embodiment, the array includes at least two sequences selected from the group consisting of SEQ ID NOs. 24-811 and SEQ ID NOs. 1600-1622, the sequences complementary to the sequences of SEQ ID NOs. 24-811 and SEQ ID NOs. 1600-1622, and fragments comprising at least 12, 15, 18, 20, 23, 25, 28, 30, 35, 40, 50, or 100 consecutive nucleotides of said sequences. In another aspect of this embodiment, the array includes at least one, three, five, ten, fifteen, or twenty sequences selected from the group consisting of SEQ ID NOs. 24-811 and SEQ ID NOs. 1600-1622, the sequences complementary to the sequences of SEQ ID NOs. 24-811 and SEQ ID NOs. 1600-1622 and fragments comprising at least 12, 15, 18, 20, 23, 25, 28, 30, 35, 40, 50, or 100 consecutive nucleotides of said sequences.

Another embodiment of the present invention is an enriched population of recombinant nucleic acids, said recombinant nucleic acids comprising an insert nucleic acid and a backbone nucleic acid, wherein at least 0.01%, 0.05%, 0.1%, 0.5%, 1%, 2%, 5%, 10%, or 20% of said insert nucleic acids in said population comprise a sequence selected from the group consisting of SEQ ID NOs. 24-811 and SEQ ID NOs. 1600-1622 and the sequences complementary to SEQ ID NOs. 24-811 and SEQ ID NOs. 1600-1622.

Another embodiment of the present invention is a purified or isolated antibody capable of specifically binding to a polypeptide comprising a sequence selected from the group consisting of SEQ ID NOs. 812-1599.

Another embodiment of the present invention is a purified or isolated antibody capable of specifically binding to a polypeptide comprising at least 6, 8, 10, 12, 15, 18, 20, 23, 25, 28, 30, 35, 40, or 50 consecutive amino acids of a sequence selected from the group consisting of SEQ ID NOs. 812-1599.

Yet, another embodiment of the present invention is an antibody composition capable of selectively binding to an epitope-containing fragment of a polypeptide comprising a contiguous span of at least 8, 10, 12, 15, 18, 20, 23, 25, 28, 30, 35, 40, or 50 amino acids of any of SEQ ID NOs. 812-1599, wherein said antibody is polyclonal or monoclonal.

Another embodiment of the present invention is a computer readable medium having stored
thereon a sequence selected from the group consisting of a nucleic acid code of SEQ ID NOs. 24-811
and 1600-1622 and a polypeptide code of SEQ ID NOs. 812-1599.

Another embodiment of the present invention is a computer system comprising a processor and a data storage device wherein said data storage device has stored thereon a sequence selected from the group consisting of a nucleic acid code of SEQID NOs. 24-811 and 1600-1622 and a polypeptide code of SEQ ID NOs. 812-1599. In one aspect of this embodiment the computer system further comprises a sequence comparer and a data storage device having reference sequences stored thereon. For example, the sequence comparer may comprise a computer program which indicates polymorphisms. In another aspect of this embodiment, the computer system further comprises an identifier which identifies features in said sequence.

Another embodiment of the present invention is a method for comparing a first sequence to a reference sequence wherein said first sequence is selected from the group consisting of a nucleic acid code of SEQID NOs. 24-811 and 1600-1622 and a polypeptide code of SEQ ID NOs. 812-1599 comprising the steps of reading said first sequence and said reference sequence through use of a computer program which compares sequences and determining differences between said first sequence and said reference sequence with said computer program. In some aspects of this embodiment, said step of determining differences between the first sequence and the reference sequence comprises identifying polymorphisms.

Another embodiment of the present invention is a method for identifying a feature in a sequence selected from the group consisting of a nucleic acid code of SEQID NOs. 24-811 and 1600-1622 and a polypeptide code of SEQ ID NOs. 812-1599 comprising the steps of reading said sequence through the use of a computer program which identifies features in sequences and identifying features in said sequence with said computer program.

Another embodiment of the present invention is a vector comprising a nucleic acid according to any one of the nucleic acids described above.

Another embodiment of the present invention is a host cell containing the above vector.

Another embodiment of the present invention is a method of making any of the nucleic acids described above comprising the steps of introducing said nucleic acid into a host cell such that said nucleic acid is present in multiple copies in each host cell and isolating said nucleic acid from said host cell.

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Another embodiment of the present invention is a method of making a nucleic acid of any of the nucleic acids described above comprising the step of sequentially linking together the nucleotides in said nucleic acids.

Another embodiment of the present invention is a method of making any of the polypeptides described above wherein said polypeptides is 150 amino acids in length or less comprising the step of sequentially linking together the amino acids in said polypeptide.

Another embodiment of the present invention is a method of making any of the polypeptides described above wherein said polypeptides is 120 amino acids in length or less comprising the step of sequentially linking together the amino acids in said polypeptides.

Brief Description of the Drawings

Figure 1 is a summary of a procedure for obtaining cDNAs which have been selected to include the 5' ends of the mRNAs from which they derived. In the first step (1), the cap of intact mRNAs is oxidized to be chemically ligated to an oligonucleotide tag. In the second step (2), a reverse transcription is performed using random primers to generate a first cDNA strand. In the third step (3), mRNAs are eliminated and the second strand synthesis is carried out using a primer contained in the oligonucleotide tag.

Figure 2 is an analysis of the 43 amino terminal amino acids of all human SwissProt proteins to determine the frequency of false positives and false negatives using the techniques for signal peptide identification described herein.

Figure 3 summarizes a general method used to clone and sequence extended cDNAs containing sequences adjacent to 5'ESTs.

Figure 4 provides a schematic description of the promoters isolated and the way they are assembled with the corresponding 5' tags.

Figure 5 describes the transcription factor binding sites present in each of the promoters of Figure 4.

Figure 6 is a block diagram of an exemplary computer system.

Figure 7 is a flow diagram illustrating one embodiment of a process 200 for comparing a new nucleotide or protein sequence with a database of sequences in order to determine the homology levels between the new sequence and the sequences in the database.

Figure 8 is a flow diagram illustrating one embodiment of a process 250 in a computer for determining whether two sequences are homologous.

Figure 9 is a flow diagram illustrating one embodiment of an identifier process 300 for detecting the presence of a feature in a sequence.

Figure 10 is a table with all of the parameters that can be used for each step of extended cDNA analysis.

Detailed Description of the Preferred Embodiment

30 I. Obtaining 5'ESTs from cDNA libraries including the 5'Ends of their Corresponding mRNAs

The 5' ESTs of the present invention were obtained from cDNA libraries including cDNAs which include the 5'end of their corresponding mRNAs. The general method used to obtain such cDNA libraries is described in Examples 1 to 5.

EXAMPLE 1

35 <u>Preparation of mRNA</u>

Total human RNAs or polyA⁺ RNAs derived from 29 different tissues were respectively purchased from LABIMO and CLONTECH and used to generate 44 cDNA libraries as described below.

The purchased RNA had been isolated from cells or tissues using acid guanidium thiocyanate-phenol-chloroform extraction (Chomczyniski and Sacchi, *Analytical Biochemistry* 162:156-159, 1987). PolyA⁺ RNA was isolated from total RNA (LABIMO) by two passes of oligo dT chromatography, as described by Aviv and Leder, *Proc. Natl. Acad. Sci. USA* 69:1408-1412, 1972) in order to eliminate ribosomal RNA.

The quality and the integrity of the polyA+ RNAs were checked. Northern blots hybridized with a globin probe were used to confirm that the mRNAs were not degraded. Contamination of the polyA⁺ mRNAs by ribosomal sequences was checked using Northern blots and a probe derived from the sequence of the 28S rRNA. Preparations of mRNAs with less than 5% of rRNAs were used in library construction. To avoid constructing libraries with RNAs contaminated by exogenous sequences (prokaryotic or fungal), the presence of bacterial 16S ribosomal sequences or of two highly expressed fungal mRNAs was examined using PCR.

EXAMPLE 2

Methods for Obtaining mRNAs having Intact 5' Ends

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Following preparation of the mRNAs from various tissues as described above, selection of mRNA with intact 5' ends and specific attachment of an oligonucleotide tag to the 5' end of such mRNA was performed using either a chemical or enzymatic approach. Both techniques takes advantage of the presence of the "cap" structure, which characterizes the 5'end of intact mRNAs and which comprises a guanosine generally methylated once, at the 7 position. The chemical approach is illustrated in Figure 1.

The chemical modification approach involves the optional elimination of the 2', 3'-cis diol of the 3' terminal ribose, the oxidation of the 2', 3', -cis diol of the ribose linked to the cap of the 5' ends of the mRNAs into a dialdehyde, and the coupling of the such obtained dialdehyde to a derivatized oligonucleotide tag. Further detail regarding the chemical approaches for obtaining mRNAs having intact 5' ends are disclosed in International Application No. WO96/34981, published November 7, 1996.

The enzymatic approach for ligating the oligonucleotide tag to the 5' ends of mRNAs with intact 5' ends involves the removal of the phosphate groups present on the 5' ends of uncapped incomplete mRNAs, the subsequent decapping of mRNAs with intact 5' ends and the ligation of the phosphate present at the 5' end of the decapped mRNA to an oligonucleotide tag. Further detail regarding the enzymatic approaches for obtaining mRNAs having intact 5' ends are disclosed in Dumas Milne Edwards J.B. (Doctoral Thesis of Paris VI University, Le clonage des ADNc complets: difficultes et perspectives nouvelles. Apports pour l'etude de la regulation de l'expression de la tryptophane hydroxylase de rat, 20 Dec. 1993), EP0 625572 and Kato et al., Gene 150:243-250 (1994).

In either the chemical or the enzymatic approach, the oligonucleotide tag has a restriction

35 enzyme site (e.g. EcoRI sites) therein to facilitate later cloning procedures. Following attachment of the oligonucleotide tag to the mRNA, the integrity of the mRNA was then examined by performing a Northern blot using a probe complementary to the oligonucleotide tag.

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EXAMPLE 3

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cDNA Synthesis Using mRNA Templates Having Intact 5' Ends

For the mRNAs joined to oligonucleotide tags, first strand cDNA synthesis was performed using a reverse transcriptase with random nonamers as primers. In order to protect internal EcoRI sites in the cDNA from digestion at later steps in the procedure, methylated dCTP was used for first strand synthesis. After removal of mRNA by an alkaline hydrolysis, the first strand of cDNA was precipitated using isopropanol in order to eliminate residual primers.

The second strand of the cDNA was synthesized with a Klenow fragment using a primer corresponding to the 5'end of the ligated oligonucleotide. Methylated dCTP was also used for second strand synthesis in order to protect internal EcoRI sites in the cDNA from digestion during the cloning process.

EXAMPLE 4

Cloning of cDNAs derived from mRNA with intact 5' ends into BlueScript

Following second strand synthesis, the ends of the cDNA were blunted with T4 DNA polymerase (Biolabs) and the cDNA was digested with EcoRI. Since methylated dCTP was used during cDNA synthesis, the EcoRI site present in the tag was the only hemi-methylated site, hence the only site susceptible to EcoRI digestion. The cDNA was then size fractionated using exclusion chromatography (AcA, Biosepra) and fractions corresponding to cDNAs of more than 150 bp were pooled and ethanol precipitated. The cDNA was directionally cloned into the SmaI and EcoRI ends of the phagemid pBlueScript vector (Stratagene). The ligation mixture was electroporated into bacteria and propagated under appropriate antibiotic selection.

25 EXAMPLE 5

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Selection of Clones Having the Oligonucleotide Tag Attached Thereto

Clones containing the oligonucleotide tag attached were then selected as follows. The plasmid DNAs containing 5' EST libraries made as described above were purified (Qiagen). A positive selection of the tagged clones was performed as follows. Briefly, in this selection procedure, the plasmid DNA was converted to single stranded DNA using gene II endonuclease of the phage F1 in combination with an exonuclease (Chang et al., Gene 127:95-8, 1993) such as exonuclease III or T7 gene 6 exonuclease. The resulting single stranded DNA was then purified using paramagnetic beads as described by Fry et al., Biotechniques, 13: 124-131, 1992. In this procedure, the single stranded DNA was hybridized with a biotinylated oligonucleotide having a sequence corresponding to the 3' end of the oligonucleotide tag.

Clones including a sequence complementary to the biotinylated oligonucleotide were captured by incubation with streptavidin coated magnetic beads followed by magnetic selection. After capture of the positive clones, the plasmid DNA was released from the magnetic beads and converted into double

stranded DNA using a DNA polymerase such as the Thermosequenase obtained from Amersham Pharmacia Biotech. The double stranded DNA was then electroporated into bacteria. The percentage of positive clones having the 5' tag oligonucleotide was estimated using dot blot analysis to typically be between 90 and 98%.

Following electroporation, the libraries were ordered in 384-microtiter plates (MTP). A copy of the MTP was stored for future needs. Then the libraries were transferred into 96 MTP and sequenced as described below.

EXAMPLE 6

10 <u>Sequencing of Inserts in Selected Clones</u>

Plasmid inserts were first amplified by PCR on PE-9600 thermocyclers (Perkin-Elmer, Applied Biosystems Division, Foster City, CA), using standard SETA-A and SETA-B primers (Genset SA), AmpliTaqGold (Perkin-Elmer), dNTPs (Boehringer), buffer and cycling conditions as recommended by the Perkin-Elmer Corporation.

PCR products were then sequenced using automatic ABI Prism 377 sequencers (Perkin Elmer). Sequencing reactions were performed using PE 9600 thermocyclers with standard dye-primer chemistry and ThermoSequenase (Amersham Pharmacia Biotech). The primers used were either T7 or 21M13 (available from Genset SA) as appropriate. The primers were labeled with the JOE, FAM, ROX and TAMRA dyes. The dNTPs and ddNTPs used in the sequencing reactions were purchased from Boehringer. Sequencing buffer, reagent concentrations and cycling conditions were as recommended by Amersham.

Following the sequencing reaction, the samples were precipitated with ethanol, resuspended in formamide loading buffer, and loaded on a standard 4% acrylamide gel. Electrophoresis was performed for 2.5 hours at 3000V on an ABI 377 sequencer, and the sequence data were collected and analyzed using the ABI Prism DNA Sequencing Analysis Software, version 2.1.2.

EXAMPLE 7

Obtaining 5' ESTs from Extended cDNA libraries

Obtained from mRNA with Intact 5' Ends

Alternatively, 5'ESTs may be isolated from other cDNA or genomic DNA libraries. Such cDNA or genomic DNA libraries may be obtained from a commercial source or made using other techniques familiar to those skilled in the art. One example of such cDNA library construction, a full-length cDNA library, is as follows.

PolyA+ RNAs are prepared and their quality checked as described in Example 1. Then, the

caps at the 5' ends of the polyA+ RNAs are specifically joined to an oligonucleotide tag as described in

Example 2. The oligonucleotide tag may contain a restriction site such as Eco RI to facilitate further

subcloning procedures. Northern blotting is then performed to check the size of mRNAs having the oligonucleotide tag attached thereto and to ensure that the mRNAs are actually tagged.

First strand synthesis is subsequently carried out for mRNAs joined to the oligonucleotide tag as described in Example 3 above except that the random nonamers are replaced by an oligo-dT primer. For instance, this oligo-dT primer may contain an internal tag of 4 nucleotides which is different from one tissue to the other. Following second strand synthesis using a primer contained in the oligonucleotide tag attached to the 5' end of mRNA, the blunt ends of the obtained double stranded full-length DNAs are modified into cohesive ends to facilitate subcloning. For example, the extremities of full-length cDNAs may be modified to allow subcloning into the Eco RI and Hind III sites of a Bluescript vector using the Eco RI site of the oligonucleotide tag and the addition of a Hind III adaptor to the 3' end of full-length cDNAs.

The full-length cDNAs are then separated into several fractions according to their sizes using techniques familiar to those skilled in the art. For example, electrophoretic separation may be applied in order to yield 3 or 6 different fractions. Following gel extraction and purification, the cDNA fractions are subcloned into appropriate vectors, such as Bluescript vectors, transformed into competent bacteria and propagated under appropriate antibiotic conditions. Subsequently, plasmids containing tagged full-length cDNAs are positively selected as described in Example 5.

The 5' end of full-length cDNAs isolated from such cDNA libraries may then be sequenced as described in Example 6 to yield 5'ESTs.

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II. Computer Analysis of the Isolated 5' ESTs: Construction of the SignalTag™ Database

The sequence data from the cDNA libraries made as described above were transferred to a database, where quality control and validation steps were performed. A base-caller, working using a Unix system, automatically flagged suspect peaks, taking into account the shape of the peaks, the inter25 peak resolution, and the noise level. The base-caller also performed an automatic trimming. Any stretch of 25 or fewer bases having more than 4 suspect peaks was considered unreliable and was discarded. Sequences corresponding to cloning vector or ligation oligonucleotides were automatically removed from the EST sequences. However, the resulting EST sequences may contain 1 to 5 bases belonging to the above mentioned sequences at their 5' end. If needed, these can easily be removed on a case to case basis.

Following sequencing as described above, the sequences of the 5' ESTs were entered in a database for storage and manipulation as described below. Before searching the ESTs in the database for sequences of interest, ESTs derived from mRNAs which were not of interest were identified. Briefly, such undesired sequences may be of three types. First, contaminants of either endogenous (ribosomal RNAs, transfert RNAs, mitochondrial RNAs) or exogenous (prokaryotic RNAs and fungal RNAs) origins were identified. Second, uninformative sequences, namely redundant sequences, small sequences and highly degenerate sequences were identified. Third, repeated sequences (Alu, L1, THE

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and MER repeats, SSTR sequences or satellite, micro-satellite, or telomeric repeats) were identified and masked in further processing.

In order to determine the accuracy of the sequencing procedure as well as the efficiency of the 5' selection described above, the analyses described in Examples 8 and 9 respectively were performed 5 on 5'ESTs obtained from the database following the elimination of endogenous and exogenous contaminants and following the masking of repeats.

EXAMPLE 8

Measurement of Sequencing Accuracy by Comparison to Known Sequences

To further determine the accuracy of the sequencing procedure described in Example 6, the sequences of 5' ESTs derived from known sequences were identified and compared to the original known sequences. First, a FASTA analysis with overhangs shorter than 5 bp on both ends was conducted on the 5' ESTs to identify those matching an entry in the public human mRNA database available at the time of filing the priority applications. The 5' ESTs which matched a known human 15 mRNA were then realigned with their cognate mRNA and dynamic programming was used to include substitutions, insertions, and deletions in the list of "errors" which would be recognized. Errors occurring in the last 10 bases of the 5' EST sequences were ignored to avoid the inclusion of spurious cloning sites in the analysis of sequencing accuracy. This analysis revealed that the sequences incorporated in the database had an accuracy of more than 99.5%.

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EXAMPLE 9

Determination of Efficiency of 5' EST Selection

To determine the efficiency at which the above selection procedures isolated 5' ESTs which included sequences close to the 5' end of the mRNAs from which they derived, the sequences of the 25 ends of the 5' ESTs derived from the elongation factor 1 subunit α and ferritin heavy chain genes were compared to the known cDNA sequences of these genes. Since the transcription start sites of both genes are well characterized, they may be used to determine the percentage of derived 5' ESTs which included the authentic transcription start sites. For both genes, more than 95% of the obtained 5' ESTs actually included sequences close to or upstream of the 5' end of the corresponding mRNAs.

To extend the analysis of the reliability of the procedures for isolating 5' ESTs from ESTs in the database, a similar analysis was conducted using a database composed of human mRNA sequences extracted from GenBank database release 97 for comparison. The 5' ends of more than 85% of 5' ESTs derived from mRNAs included in the GenBank database were located close to the 5' ends of the known sequence. As some of the mRNA sequences available in the GenBank database are deduced from 35 genomic sequences, a 5' end matching with these sequences will be counted as an internal match. Thus, the method used here underestimates the yield of ESTs including the authentic 5' ends of their corresponding mRNAs.

EXAMPLE 10

Calculation of Novelty Indices for 5'EST Libraries

In order to evaluate the novelty of 5'EST libraries, the following analysis was performed. For each sequenced 5'EST library, the sequences were clustered by the 5' end. Each sequence in the library was compared to the others and the longest sequence found in the cluster was used as representative of the group. A novelty rate (NR) was then defined as: NR= 100 X (Number of new unique sequences found in the library/Total number of sequences from the library). Typically, novelty rating ranged between 10% and 41% depending on the tissue from which the 5'EST library was obtained. For most of the libraries, the random sequencing of 5' EST libraries was pursued until the novelty rate reached 20%.

EXAMPLE 11

Generation of Consensus Contigated 5' ESTs

Since the cDNA libraries made above include multiple 5' ESTs derived from the same mRNA, overlapping 5'ESTs may be assembled into continuous sequences. The following method describes how to efficiently align multiple 5'ESTs in order to yield not only consensus contigated 5'EST sequences for mRNAs derived from different genes but also consensus contigated 5'EST sequences for different mRNAs, so called variants, transcribed from the same gene such as alternatively spliced mRNAs.

The whole set of sequences was first partitioned into small clusters containing sequences
which exhibited perfect matches with each other on a given length and which derived from a small number of different genes. Some 5'EST sequences, so called singletons, were not aligned using this approach because they were not homologous to any other sequence.

Thereafter, all variants of a given gene were identified in each cluster using a proprietary software. 5'EST sequences belonging to the same variant were then contigated and consensus contigated 5'EST sequences generated for each variant. All consensus contigated 5' EST sequences were subsequently compared to the whole set of individual 5'EST sequences used to obtained them.

If desired, the consensus contigated 5'EST sequences may be verified by identifying clones in nucleic acid samples derived from biological tissues, such as cDNA libraries, which hybridize to the probes based on the sequences of the consensus contigated 5'ESTs using any methods described herein and sequencing those clones.

Application of this alignment method to a selected set of 5'ESTs free from endogenous contaminants and uninformative sequences, and following the masking of repeats, yielded consensus contigated 5'EST sequences or variants of clustered genes encompassing many individual 5'ESTs. Both non aligned 5'ESTs, *i.e.* singletons, and consensus contigated 5'ESTs were then compared to already known sequences and those sequences matching human mRNA sequences were eliminated from further analysis.

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EXAMPLE 12

Identification of Open Reading Frames in 5' ESTs

Subsequently, consensus contigated 5'ESTs and 5'ESTs were screened to identify those having an open reading frame (ORF).

Such open reading frames were simply defined as uninterrupted nucleic acid sequences longer than 45 nucleotides and beginning with an ATG codon.

Alternatively, the nucleic acid sequence was first divided into several subsequences which coding propensity was evaluated separately using one or several different methods known to those skilled in the art such as the evaluation of N-mer frequency and its variants (Fickett and Tung, 10 Nucleic Acids Res; 20:6441-50 (1992)) or the Average Mutual Information method (Grosse et al., International Conference on Intelligent Systems for Molecular Biology, Montreal, Canada. June 28-July 1, 1998). Each of the scores obtained by the techniques described above were then normalized by their distribution extremities and then fused using a neural network into a unique score that represents the coding probability of a given subsequence. The coding probability scores obtained for 15 each subsequence, thus the probability score profiles obtained for each reading frame, was then linked to the initiation codons present on the sequence. For each open reading frame, defined as a nucleic acid sequence beginning with an ATG codon, an ORF score was determined. Preferably, this score is the sum of the probability scores computed for each subsequence corresponding to the considered ORF in the correct reading frame corrected by a function that negatively accounts for 20 locally high score values and positively accounts for sustained high score values. The most probable ORF with the highest score was selected.

In some embodiments, nucleic acid sequences encoding an "incomplete ORF", as referred therein, namely an open reading frame in which a start codon has been identified but no stop codon has been identified, were obtained.

In other embodiments, nucleic acid sequences encoding a "complete ORF", as used therein, 25 namely an open reading frame in which a start codon and a stop codon have been identified, are obtained.

In a preferred embodiment, open reading frames encoding polypeptides of at least 50 amino acids were obtained.

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To confirm that the chosen ORF actually encodes a polypeptide, the consensus contigated 5'EST or 5'EST may be used to obtain an extended cDNA using any of the techniques described therein, and especially those described in Examples 19 and 20. Then, such obtained extended cDNAs may be screened for the most probable open reading frame using any of the techniques described therein. The amino acid sequence of the ORF encoded by the consensus contigated 5'EST or 5'EST may then be 35 compared to the amino acid sequence of the ORF encoded by the extended cDNA using any of the algorithms and parameters described therein in order to determine whether the ORF encoded by the extended cDNA is basically the same as the one encoded by the consensus contigated 5'EST or 5'EST.

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Alternatively, to confirm that the chosen ORF actually encodes a polypeptide, the consensus contigated 5'EST or 5'EST may be used to obtain an extended cDNA using any of the techniques described therein, and especially those described in Examples 19 and 20. Such an extended cDNA may then be inserted into an appropriate expression vector and used to express the polypeptide encoded by 5 the extended cDNA as described therein. The expressed polypeptide may be isolated, purified, or enriched as described therein. Several methods known to those skilled in the art may then be used to determine whether the expressed polypeptide is the one actually encoded by the chosen ORF, therein referred to an the expected polypeptide. Such methods are based on the determination of predictable features of the expressed polypeptide, including but not limited to its amino acid sequence, its size or its 10 charge, and the comparison of these features to those predicted for the expected polypeptide. following paragraphs present examples of such methods.

One of these methods consists in the determination of at least a portion of the amino acid sequence of the expressed polypeptide using any technique known to those skilled in the art. For example, the amino-terminal residues may be determined using techniques either based on Sanger's 15 technique of acid hydrolysis of a polypeptide which N-terminal residue has been covalently labeled or using techniques based on Edman degradation of polypeptides which N-terminal residues are sequentially labeled and cleaved from the polypeptide of interest. The amino acid sequence of the expressed polypeptide may then be compared to the one predicted for the expected polypeptide using any algorithm and parameters described therein.

Alternatively, the size of the expressed polypeptides may be determined using techniques familiar to those skilled in the art such as Coomassie blue or silver staining and subsequently compared to the size predicted for the expected polypeptide. Generally, the band corresponding to the expressed polypeptide will have a mobility near that expected based on the number of amino acids in the open reading frame of the extended cDNA. However, the band may have a mobility different than that 25 expected as a result of modifications such as glycosylation, ubiquitination, or enzymatic cleavage.

Alternatively, specific antibodies or antipeptides may be generated against the expected polypeptide as described in Example 34 and used to perform immunoblotting or immunoprecipitation studies against the expressed polypeptide. The presence of a band in samples from cells containing the expression vector with the extended cDNA which is absent in samples from cells containing the 30 expression vector encoding an irrelevant polypeptide indicates that the expected polypeptide or portion thereof is being expressed. Generally, the band corresponding to the expressed polypeptide will have a mobility near that expected based on the number of amino acids in the open reading frame of the extended cDNA. However, the band may have a mobility different than that expected as a result of modifications such as glycosylation, ubiquitination, or enzymatic cleavage

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The 5'ESTs or consensus contigated 5'ESTs found to encode an ORF were then searched to identify potential signal motifs using slight modifications of the procedures disclosed in Von Heijne, Nucleic Acids Res. 14:4683-4690, 1986. Those sequences encoding a 15 amino acid long stretch with a score of at least 3.5 in the Von Heijne signal peptide identification matrix were considered to possess a signal sequence. Those nucleic acid sequences which match a known human mRNA or EST sequence and have a 5' end located downstream of the known 5' end, preferably by more than 20 nucleotides, were excluded from further analysis. The remaining nucleic acids having signal sequences therein were included in a database called SignalTagTM.

10 EXAMPLE 14

Confirmation of Accuracy of Identification of Potential Signal Sequences in 5' ESTs

The accuracy of the above procedure for identifying signal sequences encoding signal peptides was evaluated by applying the method to the 43 amino acids located at the N terminus of all human SwissProt proteins. The computed Von Heijne score for each protein was compared with the known characterization of the protein as being a secreted protein or a non-secreted protein. In this manner, the number of non-secreted proteins having a score higher than 3.5 (false positives) and the number of secreted proteins having a score lower than 3.5 (false negatives) could be calculated.

Using the results of the above analysis, the probability that a peptide encoded by the 5' region of the mRNA is in fact a genuine signal peptide based on its Von Heijne's score was calculated based on either the assumption that 10% of human proteins are secreted or the assumption that 20% of human proteins are secreted. The results of this analysis are shown in Figure 2.

Using the above method of identification of secretory proteins, 5' ESTs of the following polypeptides known to be secreted were obtained: human glucagon, gamma interferon induced monokine precursor, secreted cyclophilin-like protein, human pleiotropin, and human biotinidase precursor. Thus, the above method successfully identified those 5' ESTs which encode a signal peptide.

To confirm that the signal peptide encoded by the 5' ESTs or consensus contigated 5' ESTs actually functions as a signal peptide, the signal sequences from the 5' ESTs or consensus contigated 5' ESTs may be cloned into a vector designed for the identification of signal peptides. Such vectors are designed to confer the ability to grow in selective medium only to host cells containing a vector with an operably linked signal sequence. For example, to confirm that a 5' EST or consensus contigated 5' EST encodes a genuine signal peptide, the signal sequence of the 5' EST or consensus contigated 5' EST may be inserted upstream and in frame with a non-secreted form of the yeast invertase gene in signal peptide selection vectors such as those described in U.S. Patent No. 5,536,637. Growth of host cells containing signal sequence selection vectors with the correctly inserted 5' EST or consensus contigated 5' EST signal sequence confirms that the 5' EST or consensus contigated 5' ESTs encodes a genuine signal peptide.

Alternatively, the presence of a signal peptide may be confirmed by cloning the extended cDNAs obtained using the ESTs or consensus contigated 5' ESTs into expression vectors such as pXT1 as described below, or by constructing promoter-signal sequence-reporter gene vectors which encode fusion proteins between the signal peptide and an assayable reporter protein. After introduction of these vectors into a suitable host cell, such as COS cells or NIH 3T3 cells, the growth medium may be harvested and analyzed for the presence of the secreted protein. The medium from these cells is compared to the medium from control cells containing vectors lacking the signal sequence or extended cDNA insert to identify vectors which encode a functional signal peptide or an authentic secreted protein.

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EXAMPLE 15

Analysis of the Sequences of the Invention

The set of the nucleic acid sequences of the invention (SEQ ID NOs.24-811 and 1600-1622) was obtained as described in Example 11. Subsequently, the most probable open reading frame was determined and signal sequences were searched, as described in Examples 12 and 13, for all sequences of the invention.

The nucleotide sequences of the SEQ ID NOs. 24-811 and 1600-1622 and the polypeptides sequences encoded by SEQ ID NOs. 24-811 (i.e. polypeptide sequences of SEQ ID NOs. 812-1599) are provided in the appended sequence listing which structure is as follows.

SEQ ID NOs. 24-728 are nucleic acids having an incomplete ORF which encodes a signal peptide. The locations of the incomplete ORFs and sequences encoding signal peptides are listed in the accompanying Sequence Listing. In addition, the von Heijne score of the signal peptide computed as described in Example 13 is listed as the "score" in the accompanying Sequence Listing. The sequence of the signal-peptide is listed as "seq" in the accompanying Sequence Listing. The "/" in the signal peptide sequence indicates the location where proteolytic cleavage of the signal peptide occurs to generate a mature protein.

SEQ ID NOs. 729-765 are nucleic acids having an incomplete ORF in which no sequence encoding a signal peptide has been identified to date. However, it remains possible that subsequent analysis will identify a sequence encoding a signal peptide in these nucleic acids. The locations of the incomplete ORFs are listed in the accompanying Sequence Listing.

SEQ ID NOs. 766-792 are nucleic acids having a complete ORF which encodes a signal peptide. The locations of the complete ORFs and of the signal peptides, the von Heijne score of the signal peptide, the sequence of the signal-peptide and the proteolytic cleavage site are indicated as described above.

35 SEQ ID NOs. 793-811 are nucleic acids having a complete ORF in which no sequence encoding a signal peptide has been identified to date. However, it remains possible that subsequent analysis will

identify a sequence encoding a signal peptide in these nucleic acids. The locations of the complete ORFs are listed in the accompanying Sequence Listing.

SEQ ID NOs. 812-1516 are "incomplete polypeptide sequences" which include a signal peptide. "Incomplete polypeptide sequences" are polypeptide sequences encoded by nucleic acids in which a start 5 codon has been identified but no stop codon has been identified. These polypeptides are encoded by the nucleic acids of SEQ ID NOs. 24-728. The location of the signal peptide, the von Heijne score of the signal peptide, the sequence of the signal-peptide and the proteolytic cleavage site are indicated as described above.

SEQ ID NOs. 1517-1553 are incomplete polypeptide sequences in which no signal peptide has 10 been identified to date. However, it remains possible that subsequent analysis will identify a signal peptide in these polypeptides. These polypeptides are encoded by the nucleic acids of SEQ ID NOs. 729-765.

SEQ ID NOs. 1554-1580 are "complete polypeptide sequences" which include a signal peptide. "Complete polypeptide sequences" are polypeptide sequences encoded by nucleic acids in which a start 15 codon and a stop codon have been identified. These polypeptides are encoded by the nucleic acids of SEQ ID NOs. 766-792. The location of the signal peptide, the von Heijne score of the signal peptide, the sequence of the signal-peptide and the proteolytic cleavage site are indicated as described above..

SEQ ID NOs. 1581-1599 are complete polypeptide sequences in which no signal peptide has been identified to date. However, it remains possible that subsequent analysis will identify a signal 20 peptide in these polypeptides. These polypeptides are encoded by the nucleic acids of SEQ ID NOs.793-811.

SEQ ID NOs. 1600-1622 are nucleic acid sequences in which no open reading frame has been conclusively identified to date. However, it remains possible subsequent analysis will identify an open reading frame in these nucleic acids.

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In the accompanying Sequence Listing, all instances of the symbol "n" in the nucleic acid sequences mean that the nucleotide can be adenine, guanine, cytosine or thymine. In some instances the polypeptide sequences in the Sequence Listing contain the symbol "Xaa." These "Xaa" symbols indicate either (1) a residue which cannot be identified because of nucleotide sequence ambiguity or (2) a stop codon in the determined sequence where applicants believe one should not exist (if the sequence 30 were determined more accurately). In some instances, several possible identities of the unknown amino acids may be suggested by the genetic code.

In the case of secreted proteins, it should be noted that, in accordance with the regulations governing Sequence Listings, in the appended Sequence Listing, the full protein (i.e. the protein containing the signal peptide and the mature protein) extends from an amino acid residue having a 35 negative number through a positively numbered C-terminal amino acid residue. Thus, the first amino acid of the mature protein resulting from cleavage of the signal peptide is designated as amino acid

number 1, and the first amino acid of the signal peptide is designated with the appropriate negative

If one of the nucleic acid sequences of SEQ ID NOs. 24-811 and 1600-1622 are suspected of containing one or more incorrect or ambiguous nucleotides, the ambiguities can readily be resolved by resequencing a fragment containing the nucleotides to be evaluated. If one or more incorrect or ambiguous nucleotides are detected, the corrected sequences should be included in the clusters from which the sequences were isolated, and used to compute other consensus contigated sequences on which other ORFs would be identified. Nucleic acid fragments for resolving sequencing errors or ambiguities may be obtained from deposited clones or can be isolated using the techniques described herein.

10 Resolution of any such ambiguities or errors may be facilitated by using primers which hybridize to sequences located close to the ambiguous or erroneous sequences. For example, the primers may hybridize to sequences within 50-75 bases of the ambiguity or error. Upon resolution of an error or ambiguity, the corresponding corrections can be made in the protein sequences encoded by the DNA containing the error or ambiguity. The amino acid sequence of the protein encoded by a particular clone can also be determined by expression of the clone in a suitable host cell, collecting the protein, and determining its sequence.

In addition, if one of the sequences of SEQ ID NOs. 812-1599 is suspected of containing a truncated ORF as the result of a frameshift in the sequence, such frameshifting errors may be corrected by combining the following two approaches. The first one involves thorough examination of all double predictions, *i.e.* all cases where the probability scores for two ORFs located on different reading frames are high and close, preferably different by less than 0.4. The fine examination of the region where the two possible ORFs overlap may help to detect the frameshift. In the second approach, homologies with known proteins are used to correct suspected frameshifts.

Of the identified clusters, some were shown to be multivariant, *i.e.* to contain several variants of the same gene. Table I gives for each of the multivariant clusters named by its internal reference (first column), the list of all variant consensus contigated 5'ESTs (second column), each being represented by a different sequence identification number.

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number.

TABLE I

Cluster Internal Reference	SEQ ID NOs of Variants
C1	687, 791
C2	744, 798
C3	640, 811
. C4	59, 66
C5	84, 97 .

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C6	287, 289	
C7	286, 775, 777	
C8	762, 768	
C9	783, 784	
C10	80, 1603	
C11	655, 736	
C12	805, 806	

Table II provides a list preferred polynucleotide fragments which are derivatives of the consensus contigated 5'ESTs. As used herein the term "polynucleotide described in Table II" refers to the all of the preferred polynucleotide fragments defined in Table II in the following manner. The fragments are referred to by their SEQ ID numbers in the first column. The preferred polynucleotide fragments are then defined by a range of nucleotide positions from the SEQ IDs of the consensus contigated 5'ESTs as indicated in the second column entitled "positions of preferred fragments." The preferred polynucleotide fragments correspond to the individual 5'ESTs aligned to obtain the consensus contigated 5'EST and to those filed in the priority documents. The third column entitled "variant nucleotides" describes the nucleotide sequence variations observed between the consensus contigated 5'EST and preferred nucleic acid fragments as follows:

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A) Substitutions in the sequence of a consensus contigated 5'EST to derive a preferred polynucleotide fragment are denoted by an "S", followed by a number indicating the first nucleotide position in a specific SEQ ID to be substituted in a string of substituted nucleotides or the position of the substituted nucleotide in the case of a single substituted nucleotide. Then there is a coma followed by one or more lower case letters indicating the identity of the nucleotide(s) occurring in the substituted position(s). For example, SEQ ID NO: 3401; Position of preferred fragments: 1-250; Variant nucleotides S45, atc would indicate that a preferred polynucleotide fragment had the sequence of positions 1 to 250 of SEQ ID NO. 3401, except that the nucleotides at positions 45, 46, and 47 were substituted with A, T, and C, respectively, in the preferred polynucleotide as compared with the sequence of SEQ ID No. 3401.

B) Insertions in the sequence of a consensus contigated 5'EST to derive a preferred polynucleotide fragment are denoted by an "I", followed by a number indicating the nucleotide position in a specific SEQ ID after which a string of nucleotides is inserted or the position after which the nucleotide is inserted in the case of a single inserted nucleotide. Then there is a coma followed by one or more lower case letters indicating the identity of the nucleotide(s) occurring in the inserted position(s). For example, SEQ ID NO: 7934; Position of preferred fragments: 1-500; Variant nucleotides: I36,gataca would indicate that a preferred polynucleotide fragment had the sequence of positions 1 to 500 of SEQ ID NO. 7934, except that after the nucleotides at position 36 a GATACA string of nucleotides is inserted in the preferred polynucleotide as compared with the sequence of SEQ ID No. 7934.

C) Deletions in the sequence of a consensus contigated 5'EST to derive a preferred nucleic acid fragment are denoted by an "D", followed by a number indicating the first nucleotide position in a specific SEQ ID to be deleted in a string of deleted nucleotides or the position of the deleted nucleotide in the case of a single deleted nucleotide. Then there is a coma followed by number indicating the number of nucleotide(s) deleted from the sequence provided in the sequence ID. For example, SEQ ID NO: 5398; Position of preferred fragments: 56-780; Variant nucleotides D114,5 would indicate that a preferred polynucleotide fragment had the sequence of positions 56 to 780 of SEQ ID NO. 5398, except that the nucleotides in positions 114 to 118 had been deleted in the preferred polynucleotide as compared with the sequence of SEQ ID No. 5398.

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The present invention encompasses isolated, purified, or recombinant nucleic acids which consist of, consist essentially of, or comprise a contiguous span of at least 8, 10, 12, 15, 18, 20, 25, 35, 40, 50, 70, 80, 100, 250, or 500 nucleotides in length, to the extent that a contiguous span of these lengths is consistent with the lengths of the particular polynucleotide, of a polynucleotide described in Table II, or a sequence complementary thereto, wherein said polynucleotide described in Table II is selected individually or in any combination from the polynucleotides described in Table II. The present invention also encompasses isolated, purified, or recombinant nucleic acids which consist of or consist essentially of a polynucleotide described in Table II, or a sequence complementary thereto, wherein said polynucleotide is selected individually or in any combination from the polynucleotides described in Table II. The present invention further encompasses isolated or purified polypeptides which consist of, consist essentially of, or comprise a contiguous span of at least 8, 10, 12, 15, 18, 20, 25, 35, 40, 50, 70, 80, or 100 amino acids encoded by a polynucleotide described in Table II.

Table II

SEQ ID NO.	Positions of Preferred Fragments	Variant nucleotides
35	1-423	S124, s; I135, a; S293, w; I363, a; S377, r; D424, 15
41	1-427	I117, m; S120, r; S124, g; D373, 1; S376, b; S378, b; I427, gggg; D428, 109
43	1-276	S114, m; S118, rg; S123, r; S139, nr; I142, t; D148, 1; D152, 1; I228, t; I276, gg; D277, 136
45	126-420	D1, 125; I420, ggg; D421, 100
46	1-255	S139, r; 1145, r; S146, mm; S150, ar; S254, g; D256, 128
48	4-437	D1, 3; S49, a; S55, g; S79, a; S90, a; I437, tetetg
59	1-471	S26, a; S44, t; S48, t; S109, a; S191, t; S200, gc; S203, a; S210, g; S237, a; S240, g; S255, a; S272, a; S277, a; S279, a; S284, t; S297, g; S305, g; S316, a; I471, ggtca
66	1-428	I428, tactgggg

		
82	1-399	S251, t; S277, d; I399, aagccggg
84	5-488	D1, 4; S210, g; S293, a; S325, g; S339, a;
	ļ	S348, g; S353, g; S395, g; I488, cacca
93	1-508	I508, gattt
96	26-315	D1, 25; S28, a; S62, c; I315, cagatgg
97	4-460	D1, 3; S19, g; S31, g; S114, gt; S118, a; S123,
		tc; S127, c; S132, a; S186, g; S190, c; S203, t;
		S210, g; S232, c; I460, acgtt
105	1-281	S273, a; I281, g; D282, 211
114	10-315	I0, t; D1, 9; S91, m; S267, n; S276, w; S292, h;
		S295, m; I315, tggg; D316, 19
118	1-145	S57, d; S126, d; I145, ccctc
120	2-348	D1, 1; S104, t; I348, g; D349, 38
121	1-190	I121, c; I190, ccctt
123	1-353	I117, m; I186, w; S187, y; I353, caccgggg
124	1-249	I249, ggrvgggg
125	114-375	D1, 113; S206, wn; I231, a; I375, ccctagg
126	1-437	S297, cc; S307, tg; S312, a; S318, g; S341, a;
		S351, t; S353, g; S383, c; S387, a; D404, 1
136	82-428	D1, 81; I428, aaagtg
139	1-268	I268, gggaaggg
148	6-405	D1, 5; I405, ggtgt
159	1-230	S227, ta; I230, ccctggg
165	3-256	10, tat; D1, 2; I17, c; S18, t; S111, d; I115, t;
		S123, r; I256, aaggeggg
170	1-280	I103, t; S104, c; I111, t; I280, cgttcggg
194	1-215	S50, s; S186, sn; S199, k; I215, gcagcggg
213	1-158	S128, m; I132, w; S143, d; I158, tgcccggg
223	3-431	D1, 2; S28, s; S79, c; S82, s; S308, nr; S328,
l	ł	nb; I431, ccggc
247	1-359	176, gttt; 1359, tccctgg
258	1-236	S72, r; S81, g; S197, s; I205, ss; S232, k; I236,
		actteggg
264	5-283	D1, 4; S64, g; S122, m; S134, yy; I137, c;
		1151, t; 1283, gttgc
269	1-143	S111, s; I143, ggggcggg
286	5-207	D1, 4; S204, a; S206, c; I207, gg; D208, 567
287	1-277	S114, r; I125, t; S131, ag; S256, tg; S259, tt;
		S262, at; S267, t; S269, c; S273, c; I277,
		ccggg; D278, 337
289	69-416	D1, 68; I416, agccaggg
289	1-278	S114, r; I125, t; S131, ag; S277, c; I278, cggg;
		D279, 138
292	20-254	D1, 19; I254, aaagagg
293	1-414	I414, tagcag
300	1-285	S16, m; S67, y; I285, baccacggg; D286, 1
349	23-431	D1, 22; I118, a; S214, y; I431, caactgg
350	3-386	D1, 2; S42, w; 1263, c; I386, gggat
368	3-446	D1, 2; I446, tctct
385	1-193	135, t; 1108, t; 1134, r; S135, a; S137, r; S143,
		w; I178, c; I193, gagcgggg
411	6-391	D1, 5; S17, r; S27, t; S334, y; D392, 244
412	1-185	S49, s; S127, s; I185, gctggg; D186, 150
		1

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415	2-229	D1, 1; S3, a; I229, caaatggg
435	1-386	S4, s; I386, ccggg
436	4-472	D1, 3; S61, sa; D238, 1; S239, s; I472, agtgtgg
437	1-340	1340, ggg; D341, 129
441	1-409	S109, smag; I409, cgcacggg
454	1-492	S72, nn; S115, t; S121, bwy; S181, yn; I492,
		gagtc
455	1-177	I14, w; I16, a; I177, gagctggg
459	1-311	S39, n; S74, rg; I311, accatggg
460	1-425	I425, agtac
461	5-420	D1, 4; I420, tcgtc
481	1-429	I10, w; S262, d; S333, n; I429, ctccaggg
489	1-414	D72, 1; S117, n; S396, d; I414, ggaca
496	1-215	I215, ttttcggg
501	1-430	S275, n; I430, aggat
502	91-413	D1, 90; I413, aaacgggg
504	21-420	D1, 20; S47, w; S83, n; I280, n; S281, na;
		S292, v; S314, sm; S368, ww; S373, w; I420, '
		cccca
505	18-457	D1, 17; D36, 1; S182, g; S273, n; S283, a;
		S416, bh; I457, ctcga
514	1-303	I303, accca
515	1-455	S11, t; I12, n; S30, r; S256, wr; I333, t; I455,
		cataa
517	24-453	D1, 23; I453, agagcggg
519	1-275	I119, gt; S125, w; I129, w; S133, k; S137, k;
		S167, k; I275, gcccc
522	1-313	I313, agcgtggg
526	4-366	I0, t; D1, 3; I366, ggcccggg
530	1-434	S328, g; I434, aagat
535	1-379	S128, g; S162, m; D380, 5
561	2-341	D1, 1; I341, raagagg
568	1-246	I118, g; S137, g; I246, aaaccggg
570	1-207	1207, ttttt
576	1-288	134, c; 1288, cccgtgg
588	1-390	S218, a; S224, k; S314, dh; S358, s; D376, 1;
		I390, atg; D391, 23
597	31-274	D1, 30; S49, n; I274, tccatgg
606	1-354	[1141, g; D174, 1; S229, rr; D355, 72
627	1-415	S7, a; I415, cattt
634	1-178	D179, 212
640	6-428	D1, 5; D429, 79
641	64-483	D1, 63; 1165, d; D183, 1; S185, y; S253, t;
		D279, 2; S416, a; I483, atata
655	1-280	S58, c; 184, g; S88, k; S204, ac; S244, g; S247,
		g; I280, ggg; D281, 90
672	34-489	D1, 33; S316, k; S331, k; S333, w; S486, g;
	116 122	S488, c; D490, 4
687	116-473	D1, 115; S142, n; I473, cctcgggg
697	1-202	\$142, s; \$144, sr; \$148, d; \$152, d; \$1155, a;
700	0 204	1164, a; S174, k; 1202, gcc; D203, 291
708		
710	8-384 1-167	D1, 7; S104, b; 1384, gaaaa S40, k; S49, db; I167, tatct

		34
722	1-191	I125, c; I191, ttttt
723	1-316	I316, aggg; D317, 157
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730	29-372	D1, 28; I155, g; S192, ka; S333, d; I372, m; D373, 93
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733	20-375	D1, 19; S306, sbs; I325, h; S326, nr; S338, ywd; S344, v; I375, aggg; D376, 68
734	1-359	D66, 1; D360, 14
735	25-322	D1, 24; S30, r; I193, a; I322, ccaaggg
736	9-181	D1, 8; S58, g; I181, aactaggg
737	1-160	S97, ta; I160, aggtc
738	1-227	D228, 7
739	45-514	D1, 44; S178, s; I182, c; S436, dmn; S461, v; S476, c; S506, t; D515, 75
740	11-388	D1, 10; I388, cgacaggg
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. 742	217-553	10, tt; D1, 216; S286, r; S294, m; S311, r;
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		S485, s; S491, w; I495, ht; S496, v; S513, r;
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-743	1-459	III, s; S258, m; I270, m; I304, c; I308, amta; S313, c; S438, v; I459, agggag
744	25-316	D1, 24; S315, g; D317, 95
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753	1-189	S26, r; S115, s; I121, r; S122, r; S128, s; S143,
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754	1-395	S212, wd; I395, cggca
755	19-460	D1, 18; S26, c; S156, a; S253, n; I460, tagaagg
756	2-142	D1, 1; I106, gc; S107, t; S110, c; I142,
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759	19-452	D1, 18; S421, w; I452, a
760	25-175	D1, 24; S34, yk; I175, ccggg; D176, 120
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762	1-374	S320, s; S349, a; D375, 249
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797	1-420	S136, c; S150, c; I245, ccc; I420, ggagtg
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1600 1-247 S45, m; S114, k; I122, m; S123, yc; S158, rr; S221, k; I247, ceccaggg 1601 1-225 S109, bm; S195, m; I225, tgcacggg 1602 23-245 D1, 22; D138, 1; S139, s; S242, t; S244, g; I245, g; D246, 13 1603 1-303 S71, c; D277, 1; I303, ggagggg; D304, 38 1604 1-242 S47, w; S50, c; S81, h; S85, d; S91, k; S106, r; I242, tgtggg; D243, 50 1605 2-225 D1, 1; S20, k; S91, c; I225, ggg; D226, 132 1606 15-293 D1, 14; S156, g; S193, g; I200, t; I293, acaaaggg 1607 1-361 S323, c; I361, cecca 1608 1-151 I151, taagggg; D152, 154 1609 1-242 S55, s; I135, a; S152, h; I242, cagtaggg 1610 1-196 I151, w; S190, k; I196, cetgtgg 1611 1-228 S115, k; S174, rk; I228, cgtttggg 1612 1-221 S108, v; I221, tgateggg 1613 1-281 I66, w; I137, a; D282, 79 1614 1-171 S53, k; S76, k; I80, k; S81, kw; S86, r; S92, k; S126, k; I171, gccgagg 1615 2-193 D1, 1; S67, c; I121, s; S122, mm; S126, g; S130, r; S146, r; S156, gm; I193, cetca 1616 1-349 S251, ww; S259, rs; S275, k; I279, w; S285, y; S292, y; I320, m; I331, m; I338, w; I341, s; I349, accceggg 1617 1-129 I118, t; D130, 26 1618 1-184 D9, 1; D185, 1	811	6-270	D1, 5; I270, gggg; D271, 115
S221, k; I247, ccccaggg	1600	- 1-247	
1602 23-245 D1, 22; D138, 1; S139, s; S242, t; S244, g; I245, g; D246, 13 1603 1-303 S71, c; D277, 1; I303, ggagggg; D304, 38 1604 1-242 S47, w; S50, c; S81, h; S85, d; S91, k; S106, r; I242, tgtggg; D243, 50 1605 2-225 D1, 1; S20, k; S91, c; I225, ggg; D226, 132 1606 15-293 D1, 14; S156, g; S193, g; I200, t; I293, acaaaggg 1607 1-361 S323, c; I361, cccca 1608 1-151 I151, taagggg; D152, 154 1609 1-242 S55, s; I135, a; S152, h; I242, cagtaggg 1610 1-196 I151, w; S190, k; I196, cctgtgg 1611 1-228 S115, k; S174, rk; I228, cgtttggg 1612 1-221 S108, v; I221, tgatcggg 1613 1-281 I66, w; I137, a; D282, 79 1614 1-171 S53, k; S76, k; I80, k; S81, kw; S86, r; S92, k; S126, k; I171, gccgagg 1615 2-193 D1, 1; S67, c; I121, s; S122, mm; S126, g; S130, r; S146, r; S156, gm; I193, cctca 1616 1-349 S251, ww; S259, rs; S275, k; I279, w; S285, y; S292, y; I320, m; I331, m; I338, w; I341, s; I349, accceggg 1617 1-129 I118, t; D130, 26 1618 1-184 D9, 1; D185, 1			
1602 23-245 D1, 22; D138, 1; S139, s; S242, t; S244, g; 1245, g; D246, 13 1603 1-303 S71, c; D277, 1; I303, ggagggg; D304, 38 1604 1-242 S47, w; S50, c; S81, h; S85, d; S91, k; S106, r; 1242, tgtggg; D243, 50 1605 2-225 D1, 1; S20, k; S91, c; I225, ggg; D226, 132 1606 15-293 D1, 14; S156, g; S193, g; I200, t; I293, acaaaggg 1607 1-361 S323, c; I361, cccca 1608 1-151 I151, taagggg; D152, 154 1609 1-242 S55, s; I135, a; S152, h; I242, cagtaggg 1610 1-196 I151, w; S190, k; I196, cctgtgg 1611 1-228 S115, k; S174, rk; I228, cgtttggg 1612 1-221 S108, v; I221, tgatcggg 1613 1-281 I66, w; I137, a; D282, 79 1614 1-171 S53, k; S76, k; I80, k; S81, kw; S86, r; S92, k; S126, k; I171, gccgagg 1615 2-193 D1, 1; S67, c; I121, s; S122, mm; S126, g; S130, r; S146, r; S156, gm; I193, cctca 1616 1-349 S251, ww; S259, rs; S275, k; I279, w; S285, y; S292, y; I320, m; I331, m; I338, w; I341, s; I349, acccggg 1617 1-129 I118, t; D130, 26 1618 1-184 D9, 1; D185, 1	1601	1-225	
1245, g; D246, 13	1602	23-245	
1603 1-303 S71, c; D277, 1; I303, ggagggg; D304, 38 1604 1-242 S47, w; S50, c; S81, h; S85, d; S91, k; S106, r; I242, tgtggg; D243, 50 1605 2-225 D1, 1; S20, k; S91, c; I225, ggg; D226, I32 1606 15-293 D1, 14; S156, g; S193, g; I200, t; I293, acaaaggg 1607 1-361 S323, c; I361, cccca 1608 1-151 I151, taagggg; D152, 154 1609 1-242 S55, s; I135, a; S152, h; I242, cagtaggg 1610 1-196 I151, w; S190, k; I196, cctgtgg 1611 1-228 S115, k; S174, rk; I228, cgtttggg 1612 1-221 S108, v; I221, tgatcggg 1613 1-281 I66, w; I137, a; D282, 79 1614 1-171 S53, k; S76, k; I80, k; S81, kw; S86, r; S92, k; S126, k; I171, gccgagg 1615 2-193 D1, 1; S67, c; I121, s; S122, mm; S126, g; S130, r; S146, r; S156, gm; I193, cctca 1616 1-349 S251, ww; S259, rs; S275, k; I279, w; S285, y; S292, y; I320, m; I331, m; I338, w; I341, s; I349, accceggg 1617 1-129 I118, t; D130, 26 1618 1-184 D9, 1; D185, 1			
1604 1-242 \$47, w; \$50, c; \$81, h; \$85, d; \$91, k; \$106, r; 1242, tgtggg; D243, 50 1605 2-225 D1, 1; \$20, k; \$91, c; 1225, ggg; D226, 132 1606 15-293 D1, 14; \$156, g; \$193, g; 1200, t; 1293, acaaaggg 1607 1-361 \$323, c; 1361, cccca 1608 1-151 1151, taagggg; D152, 154 1609 1-242 \$55, s; 1135, a; \$152, h; 1242, cagtaggg 1610 1-196 1151, w; \$190, k; 1196, cctgtgg 1611 1-228 \$115, k; \$174, rk; 1228, cgtttggg 1612 1-221 \$108, v; 1221, tgatcggg 1613 1-281 I66, w; 1137, a; D282, 79 1614 1-171 \$53, k; \$76, k; 180, k; \$81, kw; \$86, r; \$92, k; \$126, k; 1171, gccgagg 1615 2-193 D1, 1; \$67, c; 1121, s; \$122, mm; \$126, g; \$130, r; \$146, r; \$156, gm; 1193, cctca 1616 1-349 \$251, ww; \$259, rs; \$275, k; 1279, w; \$285, y; \$292, y; 1320, m; 1331, m; 1338, w; 1341, s; 1349, accceggg 1617 1-129 I118, t; D130, 26 1618 1-184 D9, 1; D185, 1	1603	1-303	
1605 2-225 D1, 1; S20, k; S91, c; I225, ggg; D226, 132 1606 15-293 D1, 14; S156, g; S193, g; I200, t; I293, acaaaggg 1607 1-361 S323, c; I361, cccca 1608 1-151 I151, taagggg; D152, 154 1609 1-242 S55, s; I135, a; S152, h; I242, cagtaggg 1610 1-196 I151, w; S190, k; I196, cctgtgg 1611 1-228 S115, k; S174, rk; I228, cgtttggg 1612 1-221 S108, v; I221, tgatcggg 1613 1-281 I66, w; I137, a; D282, 79 1614 1-171 S53, k; S76, k; I80, k; S81, kw; S86, r; S92, k; S126, k; I171, gccgagg 1615 2-193 D1, 1; S67, c; I121, s; S122, mm; S126, g; S130, r; S146, r; S156, gm; I193, cctca 1616 1-349 S251, ww; S259, rs; S275, k; I279, w; S285, y; S292, y; I320, m; I331, m; I338, w; I341, s; I349, accceggg 1617 1-129 I118, t; D130, 26 1618 1-184 D9, 1; D185, 1	1604	1-242	S47, w; S50, c; S81, h; S85, d; S91, k; S106, r;
1606 15-293 D1, 14; S156, g; S193, g; I200, t; I293, acaaaggg 1607 1-361 S323, c; I361, cccca 1608 1-151 I151, taagggg; D152, 154 1609 1-242 S55, s; I135, a; S152, h; I242, cagtaggg 1610 1-196 I151, w; S190, k; I196, cctgtgg 1611 1-228 S115, k; S174, rk; I228, cgtttggg 1612 1-221 S108, v; I221, tgatcggg 1613 1-281 I66, w; I137, a; D282, 79 1614 1-171 S53, k; S76, k; I80, k; S81, kw; S86, r; S92, k; S126, k; I171, gccgagg 1615 2-193 D1, 1; S67, c; I121, s; S122, mm; S126, g; S130, r; S146, r; S156, gm; I193, cctca 1616 1-349 S251, ww; S259, rs; S275, k; I279, w; S285, y; S292, y; I320, m; I331, m; I338, w; I341, s; I349, accceggg 1617 1-129 I118, t; D130, 26 1618 1-184 D9, 1; D185, 1			I242, tgtggg; D243, 50
acaaaggg 1607	1605	2-225	D1, 1; S20, k; S91, c; I225, ggg; D226, 132
1607 1-361 S323, c; I361, cccca 1608 1-151 I151, taagggg; D152, 154 1609 1-242 S55, s; I135, a; S152, h; I242, cagtaggg 1610 1-196 I151, w; S190, k; I196, cctgtgg 1611 1-228 S115, k; S174, rk; I228, cgtttggg 1612 1-221 S108, v; I221, tgatcggg 1613 1-281 I66, w; I137, a; D282, 79 1614 1-171 S53, k; S76, k; I80, k; S81, kw; S86, r; S92, k; S126, k; I171, gccgagg 1615 2-193 D1, 1; S67, c; I121, s; S122, mm; S126, g; S130, r; S146, r; S156, gm; I193, cctca 1616 1-349 S251, ww; S259, rs; S275, k; I279, w; S285, y; S292, y; I320, m; I331, m; I338, w; I341, s; I349, accccggg 1617 1-129 I118, t; D130, 26 1618 1-184 D9, 1; D185, 1	1606	15-293	D1, 14; S156, g; S193, g; I200, t; I293,
1608 1-151 I151, taagggg; D152, 154 1609 1-242 S55, s; I135, a; S152, h; I242, cagtaggg 1610 1-196 I151, w; S190, k; I196, cctgtgg 1611 1-228 S115, k; S174, rk; I228, cgtttggg 1612 1-221 S108, v; I221, tgatcggg 1613 1-281 I66, w; I137, a; D282, 79 1614 1-171 S53, k; S76, k; I80, k; S81, kw; S86, r; S92, k; S126, k; I171, gccgagg 1615 2-193 D1, 1; S67, c; I121, s; S122, mm; S126, g; S130, r; S146, r; S156, gm; I193, cctca 1616 1-349 S251, ww; S259, rs; S275, k; I279, w; S285, y; S292, y; I320, m; I331, m; I338, w; I341, s; I349, accccggg 1617 1-129 I118, t; D130, 26 1618 1-184 D9, 1; D185, 1			acaaaggg
1609 1-242 S55, s; I135, a; S152, h; I242, cagtaggg 1610 1-196 I151, w; S190, k; I196, cctgtgg 1611 1-228 S115, k; S174, rk; I228, cgtttggg 1612 1-221 S108, v; I221, tgatcggg 1613 1-281 I66, w; I137, a; D282, 79 1614 1-171 S53, k; S76, k; I80, k; S81, kw; S86, r; S92, k; S126, k; I171, gccgagg 1615 2-193 D1, 1; S67, c; I121, s; S122, mm; S126, g; S130, r; S146, r; S156, gm; I193, cctca 1616 1-349 S251, ww; S259, rs; S275, k; I279, w; S285, y; S292, y; I320, m; I331, m; I338, w; I341, s; I349, accceggg 1617 1-129 I118, t; D130, 26 1618 1-184 D9, 1; D185, 1	1607	1-361	
1610 1-196 I151, w; S190, k; I196, cctgtgg 1611 1-228 S115, k; S174, rk; I228, cgtttggg 1612 1-221 S108, v; I221, tgatcggg 1613 1-281 I66, w; I137, a; D282, 79 1614 1-171 S53, k; S76, k; I80, k; S81, kw; S86, r; S92, k; S126, k; I171, gccgagg 1615 2-193 D1, 1; S67, c; I121, s; S122, mm; S126, g; S130, r; S146, r; S156, gm; I193, cctca 1616 1-349 S251, ww; S259, rs; S275, k; I279, w; S285, y; S292, y; I320, m; I331, m; I338, w; I341, s; I349, accceggg 1617 1-129 I118, t; D130, 26 1618 1-184 D9, 1; D185, 1	1608	1-151	I151, taagggg; D152, 154
1611 1-228 S115, k; S174, rk; I228, cgtttggg 1612 1-221 S108, v; I221, tgatcggg 1613 1-281 I66, w; I137, a; D282, 79 1614 1-171 S53, k; S76, k; I80, k; S81, kw; S86, r; S92, k; S126, k; I171, gccgagg 1615 2-193 D1, 1; S67, c; I121, s; S122, mm; S126, g; S130, r; S146, r; S156, gm; I193, cctca 1616 1-349 S251, ww; S259, rs; S275, k; I279, w; S285, y; S292, y; I320, m; I331, m; I338, w; I341, s; I349, accceggg 1617 1-129 I118, t; D130, 26 1618 1-184 D9, 1; D185, 1		1-242	S55, s; I135, a; S152, h; I242, cagtaggg
1612 1-221 \$108, v; \$121, \$108 teggg 1613 1-281 \$166, w; \$1137, a; \$D282, 79 1614 1-171 \$53, k; \$76, k; \$180, k; \$81, kw; \$86, r; \$92, k; \$126, k; \$1171, \$126 teggg 1615 2-193 \$D1, 1; \$67, c; \$1121, s; \$122, mm; \$126, g; \$130, r; \$146, r; \$156, gm; \$1193, cctca 1616 1-349 \$251, ww; \$259, rs; \$275, k; \$1279, w; \$285, y; \$292, y; \$1320, m; \$1331, m; \$1338, w; \$1341, s; \$1349, accceggg 1617 1-129 \$1118, t; \$D130, \$26 1618 1-184 \$D9, 1; \$D185, \$1		1-196	
1613 1-281 I66, w; I137, a; D282, 79 1614 1-171 S53, k; S76, k; I80, k; S81, kw; S86, r; S92, k; S126, k; I171, gccgagg 1615 2-193 D1, 1; S67, c; I121, s; S122, mm; S126, g; S130, r; S146, r; S156, gm; I193, cctca 1616 1-349 S251, ww; S259, rs; S275, k; I279, w; S285, y; S292, y; I320, m; I331, m; I338, w; I341, s; I349, accceggg 1617 1-129 I118, t; D130, 26 1618 1-184 D9, 1; D185, 1	1611	1-228	S115, k; S174, rk; I228, cgtttggg
1614 1-171 S53, k; S76, k; 180, k; S81, kw; S86, r; S92, k; S126, k; I171, gccgagg 1615 2-193 D1, 1; S67, c; I121, s; S122, mm; S126, g; S130, r; S146, r; S156, gm; I193, cctca 1616 1-349 S251, ww; S259, rs; S275, k; I279, w; S285, y; S292, y; I320, m; I331, m; I338, w; I341, s; I349, accceggg 1617 1-129 I118, t; D130, 26 1618 1-184 D9, 1; D185, 1		1-221	
S126, k; I171, gccgagg 1615 2-193 D1, 1; S67, c; I121, s; S122, mm; S126, g; S130, r; S146, r; S156, gm; I193, cctca 1616 1-349 S251, ww; S259, rs; S275, k; I279, w; S285, y; S292, y; I320, m; I331, m; I338, w; I341, s; I349, accceggg 1617 1-129 I118, t; D130, 26 1618 1-184 D9, 1; D185, 1		1-281	I66, w; I137, a; D282, 79
1615 2-193 D1, 1; S67, c; I121, s; S122, mm; S126, g; S130, r; S146, r; S156, gm; I193, cetca 1616 1-349 S251, ww; S259, rs; S275, k; I279, w; S285, y; S292, y; I320, m; I331, m; I338, w; I341, s; I349, accceggg 1617 1-129 I118, t; D130, 26 1618 1-184 D9, 1; D185, 1	1614	1-171	
S130, r; S146, r; S156, gm; I193, cetea 1616 1-349 S251, ww; S259, rs; S275, k; I279, w; S285, y; S292, y; I320, m; I331, m; I338, w; I341, s; I349, acceeggg 1617 1-129 I118, t; D130, 26 1618 1-184 D9, 1; D185, 1			
1616 1-349 S251, ww; S259, rs; S275, k; I279, w; S285, y; S292, y; I320, m; I331, m; I338, w; I341, s; I349, acceeggg 1617 1-129 I118, t; D130, 26 1618 1-184 D9, 1; D185, 1	1615	2-193	
S292, y; I320, m; I331, m; I338, w; I341, s; I349, accceggg 1617 1-129 I118, t; D130, 26 1618 1-184 D9, 1; D185, 1			
I349, accceggg 1617	1616	1-349	
1617 1-129 1118, t; D130, 26 1618 1-184 D9, 1; D185, 1			
1618 1-184 D9, 1; D185, 1			
1619 1-160 1122 + 1160 gangaga			
1	1619	1-169	I122, t; I169, gcccaggg
1620 1-187 S106, k; S118, m; S122, cg; S132, k; D188, 59			
1621 1 163 Diag 1 7131 0160 - 7162 Dick 100	1621	1-153	D125, 1; I131, ttt; S152, t; I153, gg; D154, 127
7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7	1622	1-400	S43, s; I126, g; I129, y; S353, d; I400, tatat

EXAMPLE 16

Categorization of 5' ESTs and Consensus Contigated 5'ESTs

The nucleic acid sequences of the present invention (SEQ ID NOs. 24-811 and 1600-1622) were grouped based on their homology to known sequences as follows. All sequences were compared to EMBL release 57 and daily releases available at the time of filing using BLASTN. All matches with a minimum of 25 nucleotides with 90% homology were retrieved and used to compute Tables IV and V.

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In some embodiments, 5'ESTs or consensus contigated 5'ESTs nucleic acid sequence do not match any known vertebrate sequence nor any publicly available EST sequence, thus being completely new.

In other embodiments, 5'ESTs or consensus contigated 5'ESTs match a known sequence.

5 Tables III and IV gives for each sequence of the invention in this category referred to by its sequence identification number in the first column, the positions of their preferred fragments in the second column entitled "Positions of preferred fragments." As used herein the term "polynucleotide described in Table III" refers to the all of the preferred polynucleotide fragments defined in Table III in this manner, and the term "polynucleotide described in Table IV" refers to the all of the preferred polynucleotides fragments 10 defined in Table IV in this manner. The present invention encompasses isolated, purified, or recombinant nucleic acids which consist of, consist essentially of, or comprise a contiguous span of at least 8, 10, 12, 15, 18, 20, 25, 35, 40, 50, 70, 80, 100, 250, or 500 nucleotides in length, to the extent that a contiguous span of these lengths is consistent with the lengths of the particular polynucleotide, of a polynucleotide described in Table III or Table IV, or a sequence complementary thereto, wherein said 15 polynucleotide described in Table III or Talbe IV is selected individually or in any combination from the polynucleotides described in Table III or Talbe IV. The present invention also encompasses isolated, purified, or recombinant nucleic acids which consist of or consist essentially of a polynucleotide described in Table III or Table IV, or a sequence complementary thereto, wherein said polynucleotide is selected individually or in any combination from the polynucleotides described in Table III or Table IV.

Table III

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SEQ ID	Positions of preferred
NO	fragments
24	1-251
25	1-83
28	227-276
29	1-27
30	130-242, 283-315, 365-461
32	314-399
33	89-321
34	1-38
35	1-52, 171-222
36	1-30, 408-441
37	1-138
39	115-140
40	1-97
41	1-112
42	1-177
46	1-38
48	376-400
51	400-466
54	1-259
55	189-320

56	265-457
· 58	246-469
59	81-123, 418-444
60	1-348
61	78-123, 418-457
62	386-439
63	1-214
64	109-297
65	1-370
• 66	92-428
68	1-180
69	165-259
70	1-178
71	1-27
72	1-179
73	1-65, 107-192
75	1-314
77	263-388
78	1-64
79	1-149
80	101-142, 302-380
82	1-192
83	1-398
85	1-290
86	1-118, 149-336
87	1-262
88	1-149
89	1-315
90	1-74
91	1-335, 364-423
92	1-316
93	338-508
94	179-321
95	219-402
96	26-315
97	348-460
98	1-230
99	391-467
101	214-336
102	1-289
	1-383
103	
104	1-211
105	1-36
106	1-126
107	1-49
108	294-336
109	1-128
111	1-154
112	407-441
113	1-80, 139-184
114	10-79
116	1-292
117	1-304
	

	39
119	1-288
120	2-348
121	1-122
123	188-353
124	1-249
125	295-375
128	1-244
129	1-232
130	196-312
131	178-276
132	. 37-174
133	1-344
134	1-244
135	1-217
136	82-428
137	1-29, 103-155, 274-434
138	1-395
139	1-268
140	1-170
141	1-396
142	1-73, 227-357
143	1-15, 227-337
143	1-433
145	61-116
146	1-71, 179-205
147	177-300
149	
151	1-146
152	1-166
	1-382
153	1-208
154	121-251
155	1-147 1-115
157	1-115
158	
159	1-44, 80-230
160	1-346
161	1-277
162	1-235
163	1-34
164	1-195
165	19-78, 175-217
166	1-209
167	1-65
168	128-218
169	49-245
170	179-280
171	1-103
172	1-218
173	1-380
174	1-139
175	1-122
176	1-300
177	1-466
	•

	40
179	1-86
180	1-245
181	1-241
182	1-263
183	1-170
184	58-106, 399-443
185	1-427
186	1-365
187	1-260
188	1-172
189	1-150
190	161-271, 301-339
191	1-91
192	1-264
193	1-246
194	1-150
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789 1-58 790 226-268 792 129-218 794 265-431 796 5-86 797 1-34 799 1-344 802 46-477 806 64-384 807 135-301 808 2-314 810 6-39 1600 1-25 1601 1-225 1602 23-139 1603 1-294 1606 15-44 1607 1-361 1611 85-228 1612 1-221 1613 138-281 1614 65-171 1615 2-142 1616 1-46 1617 1-95 1620 1-187		
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806 64-384 807 135-301 808 2-314 810 6-39 1600 1-25 1601 1-225 1602 23-139 1603 1-294 1606 15-44 1607 1-361 1611 85-228 1612 1-221 1613 138-281 1614 65-171 1615 2-142 1616 1-46 1617 1-95 1620 1-187		
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808 2-314 810 6-39 1600 1-25 1601 1-225 1602 23-139 1603 1-294 1606 15-44 1607 1-361 1611 85-228 1612 1-221 1613 138-281 1614 65-171 1615 2-142 1616 1-46 1617 1-95 1620 1-187		
810 6-39 1600 1-25 1601 1-225 1602 23-139 1603 1-294 1606 15-44 1607 1-361 1611 85-228 1612 1-221 1613 138-281 1614 65-171 1615 2-142 1616 1-46 1617 1-95 1620 1-187		
1600 1-25 1601 1-225 1602 23-139 1603 1-294 1606 15-44 1607 1-361 1611 85-228 1612 1-221 1613 138-281 1614 65-171 1615 2-142 1616 1-46 1617 1-95 1620 1-187		
1601 1-225 1602 23-139 1603 1-294 1606 15-44 1607 1-361 1611 85-228 1612 1-221 1613 138-281 1614 65-171 1615 2-142 1616 1-46 1617 1-95 1620 1-187		
1602 23-139 1603 1-294 1606 15-44 1607 1-361 1611 85-228 1612 1-221 1613 138-281 1614 65-171 1615 2-142 1616 1-46 1617 1-95 1620 1-187		
1603 1-294 1606 15-44 1607 1-361 1611 85-228 1612 1-221 1613 138-281 1614 65-171 1615 2-142 1616 1-46 1617 1-95 1620 1-187		
1606 15-44 1607 1-361 1611 85-228 1612 1-221 1613 138-281 1614 65-171 1615 2-142 1616 1-46 1617 1-95 1620 1-187		
1607 1-361 1611 85-228 1612 1-221 1613 138-281 1614 65-171 1615 2-142 1616 1-46 1617 1-95 1620 1-187		
1611 85-228 1612 1-221 1613 138-281 1614 65-171 1615 2-142 1616 1-46 1617 1-95 1620 1-187		
1612 1-221 1613 138-281 1614 65-171 1615 2-142 1616 1-46 1617 1-95 1620 1-187		
1613 138-281 1614 65-171 1615 2-142 1616 1-46 1617 1-95 1620 1-187		
1614 65-171 1615 2-142 1616 1-46 1617 1-95 1620 1-187		
1615 2-142 1616 1-46 1617 1-95 1620 1-187		
1616 1-46 1617 1-95 1620 1-187		
1617 1-95 1620 1-187		
1620 1-187		

1021 1-136		
	1621	1-136

1622	32-280,	311-400	

Table IV

SEO ID NO	Positions of Preferred
02.42.10	Fragments
35	1-52
41	1-115
45	1-47
46	1-33
. 66	400-428
82	83-149
93	399-508
105	1-36
- 114	1-79
120	1-386
121	1-190
124	1-249
125	295-328
139	1-81, 125-268
159	1-139, 180-230
165	1-78
170	179-205, 248-280
194	1-150
213	1-158
247	1-104, 155-183, 280-359
269	31-143
350	139-386
368	228-446
385	1-72, 143-193
415	95-229
435	1-386
436	446-472
441	1-361
454	1-349
455	1-105
459	35-161, 200-311
460	1-26, 56-140
481	1-429
489	1-84
496	1-44, 84-215
501	153-430
502	1-91
504	1-63
304	1-03

	51
505	1-68
514	1-303
515	237-351
519	1-145
526	231-366
530	1-88
535	1-55
570	76-207
576	168-218, 261-288
.588	1-331
597	1-83
627	1-43
634	1-41
641	1-55, 334-483
672	1-34
687	1-129
708	1-245, 296-384
710	1-243, 230-384
710	1-191
730	1-465
731	1-43
735	1-91
737	1-160
738	1-186 1-48
739	
742	1-62, 99-248
743 744	1-315, 412-459 1-31
747	1-63
747	1-32
750	1-32
	1-139
752	1-139
753	1-193
754	
759	1-38
760	1-115
763	1-62
765	1-126
769	1-85
770	1-40
771	1-148
774	1-134
775	265-531
776	71-203
777	333-469
778	144-468
779	1-28
780	1-49
781	1-102
782	1-59
783	1-53
784	1-220, 262-390
785	1-339, 408-461

	52
786	1-28
789	1-58
791	1-126
792	1-31, 129-220
793	1-31
794	355-431
795	1-33
79 7	1-31
798	1-31
799	1-401
801.	1-117
802	1-92
806	64-384
807	1-331
808	1-351
810	1-39
1600	1-25
1603	1-341
1606	1-31
1607	1-361
1608	164-305
1611	85-228
1612	1-221
1613	112-360
1614	1-171
1615	94-193

III. Evaluation of Spatial and Temporal Expression of mRNAs Corresponding to the 5'ESTs, Consensus Contigated 5'ESTs, or EST-related nucleic acids

1617

1620

5

EXAMPLE 17

1-155

1-246

Expression Patterns of mRNAs From Which the 5'ESTs were obtained

Each of the SEQ ID NOs. 24-811 and 1600-1622 was also categorized based on the tissue from which its corresponding mRNA was obtained, as follows.

Table V shows the spatial distribution of each nucleic acid sequence of the invention (SEQ ID NOs. 24-811 and 1600-1622) referred to by its sequence identification number in the first column. In the second column entitled tissue distribution, the spatial distribution is represented by the number of individual 5'ESTs used to assemble the consensus contigated 5'ESTs for a given tissue. Each type of tissue listed in Table V is encoded by a letter. The correspondence between the letter code and the tissue type is given in Table VI.

Table V

SEQ ID NO	Tissue Distribution
24	AA:1
25	S:1
26	P:1
27	W:1
28	P:1
29	S:1
30	P:1
31	P:1
32	P:1
33	P:1
34	AB:1
35	G:3; P:1; S:1; W:3; AA:4
36	P:1
37	S:1
38	Q:1
39	P:1
40	AB:1
41	B:1; C:3; F:1; G:1; H:4; S:2; T:8; W:1; Z:1; AA:3; AC:1; AD:3
42	A:1
43	N:2
44	P:1
45	C:2; K:1; O:1; S:5
46	K:1; S:2; AA:1
47	AA:1
48	C:1; O:1; P:8
49	P:1
50	P:1
51	P:1
52	S:1
53	AA:1
54	T:1
55	P:1
56	P:1
57	P:1
58	P:1
59	P:7; T:2; Z:1
60	R:1
61	C:1
62	P:1
63	F:1
64	AA:1
65	F:1

	54
66	P:4; T:2; Z:1
67	S:1
68	AA:1
69	P:1
70	P:1
71	S:1
72	W:1
73	G:1
74	P:1
75	N:1
76	P:1
77	S:1
78	U:1
79	B:1
80	P:1
81	AC:1
82	K:1; O:1
83	G:1
84	C:1; K:2; P:29; S:2; T:1; X:2; Y:1; AA:2
85	K:1
86	C:1
87	F:1
88	AB:1
89	H:1
90	M:1
91	B:1
92	K:1
93	AC:2
94	P:1
95	M:1
96	Z:2
97	K:1; P:11; S:1; X:1; AA:1
98	W:1 X:1
99	P:1
100	AB:1
101	F:1
102	AA:1
103	K:1
105	B:4; C:6; E:2; H:3; O:2; Q:1; S:3; AC:2
106	T:1
107	0:1
107	P:1
108	G:1
110	AA:1
111	T:1
111	P:1
	F:1
113	JE-1

	D 2 O 4 V 5 O 4 V 1
114	B:3; C:4; K:5; S:4; Y:1
115	U:1
116	W:1
117	T:1
118	T:2
119	T:1
120	H:3
121	AA:3
122	K:1
123	H:2
124	AA:2
125	B:1; G:1; J:3; T:13; Y:5; AA:5; AD:2
126	H:1; P:1
127	K:1
128	F:1
129	G:1
130	P:1
131	B:1
132	AA:I
133	W:1
134	P:1
135	K:1
136	B:1; C:1
137	B:1
138	H:1
139	AC:2
140	T:1
141	B:1
142	H:1
143	T:1
144	H:1
145	B:1
146	R:1
. 147	P:1
148	C:1; H:2; O:1; S:2; T:1; AC:2
149	H:1
150	AA:1
151	W:1
152	S:1
153	F:1 .
154	M:1
155	B:1
156	R:1
157	W:1
158	T:1
159	C:1; AA:1
160	F:1
161	Н:1

	50
162	D:1
163	AA:1
164	AA:1
165	W:3
166	AA:1
167	W:1
168	F:1
169	B:1
170	G:2
171	E:1
172	B:1
173	F:1
174	B:1
175	W:1
176	K:1
177	AA:1
177	S:1
179	K:1 AA:1
180	W:1
181	
182	K:1
183	T:1
184	P:1
185	B:1
186	W:1
187	R:1
188	T:1
189	T:1
190	W:1
191	A:1
192	F:1
193	B:1
194	G:3
195	W:1
196	0:1
197	T:1
198	O:1
199	B:1
200	AA:1
201	G:1
202	B:1
203	G:1
204	P:1
205	AA:1
206	Y:1
207	Y:1
208	AA:1
209	G:1

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	31
210	H:1
211	C:1
212	H:1
213	W:2
214	Y:1
215	AB:1
216	K:1
217	M:1
218	AD:1
219	A:1
220	AA:1
221	G:1
222	G:1
223	G:1; H:2; S:2; X:1
224	G:1
225	G:1
226	B:1
227	P:1
228	0:1
229	G:1
230	T:1
231	T:1
232	K:1
233	S:1
234	0:1
235	F:1
236	T:1
237	B:1
238	W:1
239	G:1
240	R:1
241	A:1
242	W:1
243	P:1
244	H:1
245	D:1
246	C:1
247	B:2
248	P:1
249	F:1
250	AB:1
251	W:1
252	H:1
253	B:1
254	S:1
255	T:1
256	W:1
257	T:1
231	1.1

	38
258	AA:2
259	P:1
260	W:1
261	H:1
262	K:1
263	K:1
264	C:1; E:1; F:1; I:4; L:1; N:22; O:1; P:1; S:1; T:9; AA:1
265	A:1
266	T:1
267	K:1
268	H:1
269	T:2
270	T:1
271	T:1
272	B:1
273	V-1
274	T:1
275	G:1
276	AA:1
277	T:1
278	AB:1
279	T:1
280	W:1
281	F:1
282	K:1
283	H:1
284	0:1
285	W:1 ,
286	B:21; C:7; H:5; K:5; O:8; S:16; W:1; Y:3; Z:4; AA:2; AC:1
287	K:2; P:12; W:1; AC:2
288	S:1
289	K:2; P:8; W:1; AC:2
290	S:1
291	H:1
292	B:11; C:2; E:1; H:7; K:1; N:3; S:1; T:8; W:1; AA:28; AC:1
293	B:6; C:3; G:1; H:6; K:4; N:4; O:3; Q:2; S:5; T:1; U:1; V:2; Y:3; AA:1
294	B:1
295	H:1
296	AA:1
297	T:1
297	T:1
	· · · · · · · · · · · · · · · · · · ·
299	T:1
300	H:1; S:1
301	H:1
302	W:1
303	W:1
304	H:1
305	G:1

	59
306	K:1
307	H:1
308	A:1
309	H:1
310	H:1 :
311	Y:1
312	G:1
313	H:1
314	K:1
315	Y:1
316	P:1
317	H:1
318	AA:1
319	H:1
320	0:1
321	Y:1
322	B:1
323	P:1
324	P:1
325	K:1 .
326	H:1
327	H:1
328	Q:1
329	S:1
330	B:1
331	T:1
332	T:1
333	B:1
334	T:1
335	W:1
336	P:1
337	A:1
338	AA:1
339	AA:1
340	G:1
341	C:1
342	K:1
343	S:1
344	G:1
345	B:1
346	Y:1
347	G:1
348	F:1
349	AA:5
350	B:15; C:1; G:1; H:1; O:1; Q:2; S:1; X:1; Y:1
351	F:1
352	R:1
353	0:1

	60
354	H:1
355	W:1
356	F:1
357	T:1
358	S:1
359	X:1
360	T:1
361	K:1
362	K:1
363	G:1
364	K:1
365	G:1
366	AA:1
367	F:1
368	C:2; H:2; X:1
369	E:1
370	T:1
371	H:1
372	G:1
373	AA:1
374	G:1
375	F:1
376	F:1
377	R:1
378	AA:1
379	AA:1
380	C:1
381	H:1
382	T:1
383	W:1
384	S:1
385	AA:2
386	D:1
387	O:1
388	W:1
389	F:1
390	W:1
391	K:1
392	W:1
393	K:1
394	T:1
395	H:1
396	T:1
397	T:1
398	G:1
399	C:1
400	K:1 \
400	B:1
401	D.1

	. 61
402	H:1
403	B:1
404	B:1
405	H:1
406	AB:1
407	0:1
408	P:1
409	X:1
410	H:1
411	B:9; C:3; K:3; L:2; O:1; S:2; X:1; AA:1
412	G:1; S:2; V:2; W:1; Y:1; Z:1
413	W:1
414	G:1
415	B:3; C:3; F:1; G:2; H:4; J:1; K:1; O:1; P:3; S:1; V:1
416	I:1
417	F:1
418	F:1
419	F:1
420	AA:1
421	F:1
422	T:1
423	P:1
424	B:1
425	Y:1
426	W:1
427	AA:1
428	W:1
429	h:i
430	Y:1
431	J:1
432	AA:1
433	G:1
434	AA:1
435	B:3; H:1
436	B:9; G:4; H:8; K:2; O:2; W:1; Z:2; AA:2; AD:3
437	H:1; T:1
438	T:1
439	R:1
440	M:1
441	H:2
442	W:1
443	B:1
444	W:1
445	AB:1
446	F:1
447	AD:1
448	AB:1
449	N:1

450 T:1 451 W:1 452 O:1 453 AA:1 454 D:28 455 W:1 456 T:1 457 G:1 458 W:1 459 Y:4 460 B:3 461 P:2 462 K:1 463 T:1 464 H:1 465 G:1 465 G:1 466 AC:1 467 R:1 468 S:1 468 S:1 470 S:1 471 T:1 472 AA:1 474 T:1 475 S:1 476 T:1 477 AA:1 478 G:1 479 W:1 480 B:1 481 D:2 482 K:1 483 P:1 486 B:1 487 Y:1 488 H:1 489 P:1; Q:1; S:3 490 C:1 491 B:1 494 H:1 493 B:1 494 H:1 495 G:1 496 N:2 497 B:1		62
452 O:1 453 AA:1 454 D:28 455 W:1 456 T:1 457 G:1 458 W:1 459 Y:4 460 B:3 461 P:2 462 K:1 463 T:1 464 H:1 465 G:1 466 AC:1 467 R:1 468 S:1 469 B:1 470 S:1 471 T:1 472 AA:1 473 W:1 474 T:1 475 AA:1 477 AA:1 477 AA:1 478 AB:1 479 W:1 480 B:1 481 O:2 482 K:1 483 P:1 488 H:1 489 P:1; Q:1; S:3 490 C:1 491 B:1 492 H:1 493 B:1 493 B:1 494 H:1 493 B:1 494 H:1 493 B:1 494 H:1 495 G:1 496 R:2	450	T:1
453 AA:1 454 D:28 455 W:1 456 T:1 457 G:1 458 W:1 459 Y:4 460 B:3 461 P:2 462 K:1 463 T:1 465 G:1 466 AC:1 467 R:1 468 S:1 469 B:1 470 S:1 471 T:1 472 AA:1 473 W:1 474 T:1 477 AA:1 478 G:1 477 AA:1 478 G:1 481 O:2 482 K:1 483 P:1 484 W:1 485 P:1 488 H:1 488 P:1 489 P:1; Q:1; S:3 490 C:1 493 B:1 494 H:1 493 B:1 494 H:1 493 B:1	451	W:1 .
454 D:28 455 W:1 456 T:1 457 G:1 458 W:1 459 Y:4 460 B:3 461 P:2 462 K:1 463 T:1 464 H:1 465 G:1 466 AC:1 467 R:1 468 S:1 469 B:1 470 S:1 471 T:1 472 AA:1 473 W:1 474 T:1 475 S:1 476 T:1 477 AA:1 478 G:1 479 W:1 480 B:1 481 O:2 482 K:1 483 P:1 484 W:1 485 P:1 488 H:1 489 P:1; Q:1; S:3 490 C:1 491 B:1 492 H:1 493 B:1 494 H:1 499 G:1	452	0:1
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691	H:1
692	AA:1
693	S:1
694	AB:1
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696	H:1
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698	0:1
699	W:1
700	S:1
701	O:1
702	B:1
703	AB:1
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705	B:1
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1619	B:2	1
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1622	H:2	

Table VI

Tissue code	Tissue type
A·	Bone Marrow
В	Brain
С	Cancerous prostate
. D	Cerebellum
Е	Colon
F	Dystrophic muscle
G	Fetal brain
Н	Fetal kidney
I	Fetal liver
J	Heart
K	Hypertrophic prostate
L	Kidney
M	Large intestine
N ·	Liver
0	Lung
P	Lymph ganglia
Q	Lymphocytes
R	Muscle
S T	Prostate
	Ovary
U	Pancreas
V	Placenta
W	Spinal cord
X	Spleen
Y	Substantia nigra
Z	Surrenals
AA	Testis
AB	Thyroid
AC	Umbilical cord
AD	Uterus

In addition to categorizing the 5' ESTs and consensus contigated 5' ESTs with respect to their tissue of origin, the spatial and temporal expression patterns of the mRNAs corresponding to the 5' ESTs and consensus contigated 5' ESTs, as well as their expression levels, may be determined as described in Example 18 below.

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Characterization of the spatial and temporal expression patterns and expression levels of these mRNAs is useful for constructing expression vectors capable of producing a desired level of gene product in a desired spatial or temporal manner, as will be discussed in more detail below.

Furthermore, 5' ESTs and consensus contigated 5' ESTs whose corresponding mRNAs are

associated with disease states may also be identified. For example, a particular disease may result from
the lack of expression, over expression, or under expression of a mRNA corresponding to a 5' EST or
consensus contigated 5' EST. By comparing mRNA expression patterns and quantities in samples taken
from healthy individuals with those from individuals suffering from a particular disease, 5' ESTs or
consensus contigated 5' ESTs responsible for the disease may be identified.

It will be appreciated that the results of the above characterization procedures for 5' ESTs and consensus contigated 5' ESTs also apply to extended cDNAs (obtainable as described below) which contain sequences adjacent to the 5' ESTs and consensus contigated 5' ESTs. It will also be appreciated that if desired, characterization may be delayed until extended cDNAs have been obtained rather than characterizing the 5' ESTs or consensus contigated 5' ESTs themselves.

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EXAMPLE 18

Evaluation of Expression Levels and Patterns of mRNAs Corresponding to EST-Related Nucleic Acids

Expression levels and patterns of mRNAs corresponding to EST-related nucleic acids may be 20 analyzed by solution hybridization with long probes as described in International Patent Application No. WO 97/05277. Briefly, an EST-related nucleic acid, fragment of an EST-related nucleic acid, positional segment of an EST-related nucleic acid, or fragment of a positional segment of an EST-related nucleic acid corresponding to the gene encoding the mRNA to be characterized is inserted at a cloning site immediately downstream of a bacteriophage (T3, T7 or SP6) RNA polymerase promoter to produce 25 antisense RNA. Preferably, the EST-related nucleic acid, fragment of an EST-related nucleic acid, positional segment of an EST-related nucleic acid, or fragment of a positional segment of an EST-related nucleic acid is 100 or more nucleotides in length. The plasmid is linearized and transcribed in the presence of ribonucleotides comprising modified ribonucleotides (i.e. biotin-UTP and DIG-UTP). An excess of this doubly labeled RNA is hybridized in solution with mRNA isolated from cells or tissues of 30 interest. The hybridizations are performed under standard stringent conditions (40-50°C for 16 hours in an 80% formamide, 0.4 M NaCl buffer, pH 7-8). The unhybridized probe is removed by digestion with ribonucleases specific for single-stranded RNA (i.e. RNases CL3, T1, Phy M, U2 or A). The presence of the biotin-UTP modification enables capture of the hybrid on a microtitration plate coated with streptavidin. The presence of the DIG modification enables the hybrid to be detected and quantified by 35 ELISA using an anti-DIG antibody coupled to alkaline phosphatase.

The EST-related nucleic acid, fragment of an EST-related nucleic acid, positional segment of an EST-related nucleic acid, or fragment of a positional segment of an EST-related nucleic acid may also be

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tagged with nucleotide sequences for the serial analysis of gene expression (SAGE) as disclosed in UK

Patent Application No. 2 305 241 A. In this method, cDNAs are prepared from a cell, tissue, organism
or other source of nucleic acid for which gene expression patterns must be determined. The resulting
cDNAs are separated into two pools. The cDNAs in each pool are cleaved with a first restriction

5 endonuclease, called an anchoring enzyme, having a recognition site which is likely to be present at least
once in most cDNAs. The fragments which contain the 5' or 3' most region of the cleaved cDNA are
isolated by binding to a capture medium such as streptavidin coated beads. A first oligonucleotide linker
having a first sequence for hybridization of an amplification primer and an internal restriction site for a
so called tagging endonuclease is ligated to the digested cDNAs in the first pool. Digestion with the

10 second endonuclease produces short tag fragments from the cDNAs.

A second oligonucleotide having a second sequence for hybridization of an amplification primer and an internal restriction site is ligated to the digested cDNAs in the second pool. The cDNA fragments in the second pool are also digested with the tagging endonuclease to generate short tag fragments derived from the cDNAs in the second pool. The tags resulting from digestion of the first and second pools with the anchoring enzyme and the tagging endonuclease are ligated to one another to produce so called ditags. In some embodiments, the ditags are concatamerized to produce ligation products containing from 2 to 200 ditags. The tag sequences are then determined and compared to the sequences of the EST-related nucleic acid, fragment of an EST-related nucleic acid, positional segment of an EST-related nucleic acid, or fragment of a positional segment of an EST-related nucleic acid to determine which 5' ESTs, consensus contigated 5' ESTs, or extended cDNAs are expressed in the cell, tissue, organism, or other source of nucleic acids from which the tags were derived. In this way, the expression pattern of the 5' ESTs, consensus contigated 5' ESTs, or extended cDNAs in the cell, tissue, organism, or other source of nucleic acids is obtained.

Quantitative analysis of gene expression may also be performed using arrays. As used herein,
the term array means a one dimensional, two dimensional, or multidimensional arrangement of ESTrelated nucleic acids, fragments of EST-related nucleic acids, positional segments EST-related nucleic
acids, or fragments of positional segments of EST-related nucleic acids. Preferably, the EST-related
nucleic acids, fragments of EST-related nucleic acids, positional segments EST-related nucleic acids, or
fragments of positional segments of EST-related nucleic acids are at least 10, 12, 15, 18, 20, 23, 25, 28,
30, 35, 40, or 50 nucleotides in length. More preferably, the EST-related nucleic acids, fragments of
EST-related nucleic acids, positional segments EST-related nucleic acids, or fragments of positional
segments of EST-related nucleic acids are at least 100 nucleotide long. More preferably, the fragments
are more than 100 nucleotides in length. In some embodiments, the EST-related nucleic acids,
fragments of EST-related nucleic acids, positional segments EST-related nucleic acids, or fragments of
positional segments of EST-related nucleic acids may be more than 500 nucleotides long.

For example, quantitative analysis of gene expression may be performed with EST-related nucleic acids, fragments of EST-related nucleic acids, positional segments EST-related nucleic acids, or

fragments of positional segments of EST-related nucleic acids in a complementary DNA microarray as described by Schena et al. (Science 270:467-470, 1995; Proc. Natl. Acad. Sci. U.S.A. 93:10614-10619, 1996). EST-related nucleic acids, fragments of EST-related nucleic acids, positional segments ESTrelated nucleic acids, or fragments of positional segments of EST-related nucleic acids are amplified by 5 PCR and arrayed from 96-well microtiter plates onto silylated microscope slides using high-speed robotics. Printed arrays are incubated in a humid chamber to allow rehydration of the array elements and rinsed, once in 0.2% SDS for 1 min, twice in water for 1 min and once for 5 min in sodium borohydride solution. The arrays are submerged in water for 2 min at 95°C, transferred into 0.2% SDS for 1 min, rinsed twice with water, air dried and stored in the dark at 25°C.

Cell or tissue mRNA is isolated or commercially obtained and probes are prepared by a single round of reverse transcription. Probes are hybridized to 1 cm² microarrays under a 14 x 14 mm glass coverslip for 6-12 hours at 60°C. Arrays are washed for 5 min at 25°C in low stringency wash buffer (1 x SSC/0.2% SDS), then for 10 min at room temperature in high stringency wash buffer (0.1 x SSC/0.2% SDS). Arrays are scanned in 0.1 x SSC using a fluorescence laser scanning device fitted with a custom 15 filter set. Accurate differential expression measurements are obtained by taking the average of the ratios of two independent hybridizations.

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Quantitative analysis of the expression of genes may also be performed with EST-related nucleic acids, fragments of EST-related nucleic acids, positional segments EST-related nucleic acids, or fragments of positional segments of EST-related nucleic acids in complementary DNA arrays as 20 described by Pietu et al. (Genome Research 6:492-503, 1996). The EST-related nucleic acids, fragments of EST-related nucleic acids, positional segments EST-related nucleic acids, or fragments of positional segments of EST-related nucleic acids thereof are PCR amplified and spotted on membranes. Then, mRNAs originating from various tissues or cells are labeled with radioactive nucleotides. After hybridization and washing in controlled conditions, the hybridized mRNAs are detected by phospho-25 imaging or autoradiography. Duplicate experiments are performed and a quantitative analysis of differentially expressed mRNAs is then performed.

Alternatively, expression analysis of the EST-related nucleic acids, fragments of EST-related nucleic acids, positional segments EST-related nucleic acids, or fragments of positional segments of EST-related nucleic acids can be done through high density nucleotide arrays as described by Lockhart 30 et al. (Nature Biotechnology 14: 1675-1680, 1996) and Sosnowsky et al. (Proc. Natl. Acad. Sci. 94:1119-1123, 1997). Oligonucleotides of 15-50 nucleotides corresponding to sequences of EST-related nucleic acids, fragments of EST-related nucleic acids, positional segments EST-related nucleic acids, or fragments of positional segments of EST-related nucleic acids are synthesized directly on the chip (Lockhart et al., supra) or synthesized and then addressed to the chip (Sosnowsky et al., supra). 35 Preferably, the oligonucleotides are about 20 to 25 nucleotides in length.

cDNA probes labeled with an appropriate compound, such as biotin, digoxigenin or fluorescent dye, are synthesized from the appropriate mRNA population and then randomly fragmented to an

average size of 50 to 100 nucleotides. The said probes are then hybridized to the chip. After washing as described in Lockhart et al, supra and application of different electric fields (Sonowsky et al, supra.), the dyes or labeling compounds are detected and quantified. Duplicate hybridizations are performed. Comparative analysis of the intensity of the signal originating from cDNA probes on the same target 5 oligonucleotide in different cDNA samples indicates a differential expression of the mRNA corresponding to the 5' EST, consensus contigated 5' EST or extended cDNA from which the oligonucleotide sequence has been designed.

IV. Use of 5' ESTs to Clone Extended cDNAs and to Clone the Corresponding Genomic DNAs

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Once 5' ESTs or consensus contigated 5' ESTs which include the 5' end of the corresponding mRNAs have been selected using the procedures described above, they can be utilized to isolate extended cDNAs which contain sequences adjacent to the 5' ESTs or consensus contigated 5' ESTs. The extended cDNAs may include the entire coding sequence of the protein encoded by the corresponding mRNA, including the authentic translation start site. If the extended cDNA encodes a 15 secreted protein, it may contain the signal sequence, and the sequence encoding the mature protein remaining after cleavage of the signal peptide.

Extended cDNAs which include the entire coding sequence of the protein encoded by the corresponding mRNA are referred to herein as "full-length cDNAs." Alternatively, the extended cDNAs may not include the entire coding sequence of the protein encoded by the corresponding mRNA, 20 although they do include sequences adjacent to the 5'ESTs or consensus contigated 5' ESTs. In some embodiments in which the extended cDNAs are derived from an mRNA encoding a secreted protein, the extended cDNAs may include only the sequence encoding the mature protein remaining after cleavage of the signal peptide, or only the sequence encoding the signal peptide.

Examples 19 and 20 below describe a general method for obtaining extended cDNAs using 5' 25 ESTs or consensus contigated 5' ESTs and nucleic acid homologous thereto. Example 21 below describes the cloning and sequencing of several extended cDNAs, including full-length cDNAs which include the authentic 5' end of the corresponding mRNA for several secreted proteins.

The methods of Examples 19 and 20 can also be used to obtain extended cDNAs which encode less than the entire coding sequence of proteins encoded by the genes corresponding to the 5' ESTs or 30 consensus contigated 5'ESTs. In some embodiments, the extended cDNAs isolated using these methods encode at least 5,10, 15, 20, 25, 30, 35, 40, 50, 75, 100, or 150 consecutive amino acids of one of the proteins encoded by the sequences of SEQ ID NOs. 24-811 and 1600-1622. In some embodiments, the extended cDNAs isolated using these methods encode at least 5, 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, or 150 consecutive amino acids of one of the proteins encoded by the sequences of SEQ ID NOs. 24-35 811.

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General Method for Using 5' ESTs or Consensus Contigated 5'ESTs to Clone and Sequence Extended cDNAs which Include the Entire Coding Region and the Authentic 5'End of the Corresponding mRNA

The following general method may be used to quickly and efficiently isolate extended cDNAs including sequence adjacent to the sequences of the 5' ESTs or Consensus Contigated 5'ESTs used to obtain them. This method may be applied to obtain extended cDNAs for any 5' EST or consensus contigated 5' EST of the invention, including those 5' ESTs and consensus contigated 5' ESTs encoding secreted proteins. This method is illustrated in Figure 3.

1. Obtaining Extended cDNAs

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The method takes advantage of the known 5' sequence of the mRNA. A reverse transcription reaction is conducted on purified mRNA with a poly dT primer containing a nucleotide sequence at its 5' end allowing the addition of a known sequence at the end of the cDNA which corresponds to the 3' end of the mRNA. Such a primer and a commercially-available reverse transcriptase enzyme are added to a buffered mRNA sample yielding a reverse transcript anchored at the 3' polyA site of the RNAs. Nucleotide monomers are then added to complete the first strand synthesis.

After removal of the mRNA hybridized to the first cDNA strand by alkaline hydrolysis, the products of the alkaline hydrolysis and the residual poly dT primer can be eliminated with an exclusion column.

Subsequently, a pair of nested primers on each end is designed based on the known 5' sequence from the 5' EST or consensus contigated 5' EST and the known 3' end added by the poly dT primer used in the first strand synthesis. Software used to design primers are either based on GC content and melting temperatures of oligonucleotides, such as OSP (Illier and Green, *PCR Meth. Appl.* 1:124-128, 1991), or based on the octamer frequency disparity method (Griffais *et al.*, *Nucleic Acids Res.* 19: 3887-3891, 1991) such as PC-Rare (http://bioinformatics.weizmann.ac.il/software/PC-

Rare/doc/manuel.html). Preferably, the nested primers at the 5' end and the nested primers at the 3' end are separated from one another by four to nine bases. These primer sequences may be selected to have melting temperatures and specificities suitable for use in PCR.

A first PCR run is performed using the outer primer from each of the nested pairs. A second PCR run using the inner primer from each of the nested pairs is then performed on a small sample of the first PCR product. Thereafter, the primers and remaining nucleotide monomers are removed.

30 2. Sequencing Extended cDNAs or Fragments Thereof

Due to the lack of position constraints on the design of 5' nested primers compatible for PCR use using the OSP software, amplicons of two types are obtained. Preferably, the second 5' primer is located upstream of the translation initiation codon thus yielding a nested PCR product containing the entire coding sequence. Such an extended cDNA may be used in a direct cloning procedure as described in section a below. However, in some cases, the second 5' primer is located downstream of the translation initiation codon, thereby yielding a PCR product containing only part of the ORF. Such incomplete PCR products are submitted to a modified procedure described in section b below.

a) Nested PCR products containing complete ORFs

When the resulting nested PCR product contains the complete coding sequence, as predicted from the 5'EST or consensus contigated 5' EST sequence, it is directly cloned in an appropriate vector as described in section 3.

5 b) Nested PCR products containing incomplete ORFs

When the amplicon does not contain the complete coding sequence, intermediate steps are necessary to obtain both the complete coding sequence and a PCR product containing the full coding sequence. The complete coding sequence can be assembled from several partial sequences determined directly from different PCR products.

Once the full coding sequence has been completely determined, new primers compatible for PCR use are then designed to obtain amplicons containing the whole coding region. However, in such cases, 3' primers compatible for PCR use are located inside the 3' UTR of the corresponding mRNA, thus yielding amplicons which lack part of this region, i.e. the polyA tract and sometimes the polyadenylation signal, as illustrated in Figure 3. Such extended cDNAs are then cloned into an 15 appropriate vector as described in section 3.

c) Sequencing extended cDNAs

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Sequencing of extended cDNAs can be performed using a Die Terminator approach with the AmpliTag DNA polymerase FS kit available from Perkin Elmer.

In order to sequence long PCR fragments, primer walking is performed using software such as 20 OSP to choose primers and automated computer software such as ASMG (Sutton et al., Genome Science Technol. 1: 9-19, 1995) to construct contigs of walking sequences including the initial 5' tag. Preferably, primer walking is performed until the sequences of full length cDNAs are obtained.

Completion of the sequencing of a given extended cDNA fragment may be assessed by comparing the sequence length to the size of the corresponding nested PCR product. When Northern 25 blot data are available, the size of the mRNA detected for a given PCR product may also be used to finally assess that the sequence is complete. Sequences which do not fulfill these criteria are discarded and will undergo a new isolation procedure.

3. Cloning Extended cDNAs

The PCR product containing the full coding sequence is then cloned in an appropriate vector. 30 For example, the extended cDNAs can be cloned into any expression vector known in the art, such as pED6dpc2 (DiscoverEase, Genetics Institute, Cambridge, MA).

Cloned PCR products are then entirely sequenced in order to obtain at least two sequences per clone. Preferably, the sequences are obtained from both sense and antisense strands according to the aforementioned procedure with the following modifications. First, both 5' and 3' ends of cloned 35 PCR products are sequenced in order to confirm the identity of the clone. Second, primer walking is performed if the full coding coding region has not been obtained yet. Contigation is then performed using primer walking sequences for cloned products as well as walking sequences that have already

contigated for uncloned PCR products. The sequence is considered complete when the resulting contigs include the whole coding region as well as overlapping sequences with vector DNA on both ends. All the contigated sequences for each cloned amplicon are then used to obtain a consensus sequence.

5 4. Selection of Cloned Full length Sequences

a) Computer analysis of extended cDNAs

Following identification of contaminants and masking of repeats, structural features, e.g. polyA tail and polyadenylation signal, of the sequences of extended cDNAs are subsequently determined using methods known to those skilled in the art. For example, algorithm, parameters and criteria defined in Figure 10 may be used. Briefly, a polyA tail is defined as a homopolymeric stretch of at least 11 A with at most one alternative base within it. The polyA tail search is restricted to the last 20 nucleotides of the sequence and limited to stretches of 11 consecutive A's because sequencing reactions are often not readable after such a polyA stretch. To search for a polyadenylation signal, the polyA tail is clipped from the full-length sequence. The 50 nucleotides preceding the polyA tail are searched for the canonic polyadenylation AAUAAA signal allowing one mismatch to account for possible sequencing errors as well as known variation in the canonical sequence of the polyadenylation signal.

Functional features, e.g. ORFs and signal sequences, of the sequences of extended cDNAs are subsequently determined as follows. The 3 upper strand frames of extended cDNAs are searched for ORFs defined as the maximum length fragments beginning with a translation initiation codon and ending with a stop codon. ORFs encoding at least 80 amino acids are preferred. If extended cDNAs encoding secreted proteins are desired, each found ORF is then scanned for the presence of a signal peptide using the matrix method described in Example 13.

Sequences of extended cDNAs are then compared, on a nucleotidic or proteic basis, to public sequences available at the time of filing.

b) Selection of full-length cDNAs of interest

A negative selection may then be performed in order to eliminate unwanted cloned sequences resulting from either contaminants or PCR artifacts as follows. Sequences matching contaminant sequences such as vector DNA, tRNA, mtRNA, rRNA sequences are discarded as well as those encoding ORF sequences exhibiting extensive homology to repeats. Sequences obtained by direct cloning (section 1a) but lacking polyA tail may be discarded. Only ORFs ending either before the polyA tail (section 1a) or before the end of the cloned 3'UTR (section 1b) may be selected. If extended cDNAs encoding secreted proteins are desired, ORFs containing a signal peptide are considered. In addition, ORFs containing unlikely mature proteins such as mature proteins which size is less than 20 amino acids or less than 25% of the immature protein size may be eliminated.

Then, for each remaining full length cDNA containing several ORFs, a preselection of ORFs may be performed using the following criteria. The longest ORF is preferred. If extended cDNAs

encoding secreted proteins are desired and if the ORF sizes are similar, the chosen ORF is the one which signal peptide has the highest score according to Von Heijne method.

Sequences of full length cDNA clones may then be compared pairwise after masking of the repeat sequences. Full-length cDNA sequences exhibiting extensive homology may be clustered in the 5 same class. Each cluster may then be subjected to a cluster analysis that detects sequences resulting from internal priming or from alternative splicing, identical sequences or sequences with several frameshifts. A selection may be operated between clones belonging to the same class in order to detect clones encoding homologous but distinct ORFs which may be both selected if they both contain sequences of interest.

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Selection of full-length cDNA clones encoding sequences of interest may subsequently be performed using the following criteria. Structural parameters (initial tag, polyadenylation site and signal) are first checked. Then, homologies with known nucleic acids and proteins are examined in order to determine whether the clone sequence match a known nucleotide/protein sequence and, in the latter case, its covering rate and the date at which the sequence became public. If there is no extensive 15 match with sequences other than ESTs or genomic DNA, or if the clone sequence brings substantial new information, such as encoding a protein resulting from alternative splicing of an mRNA coding for an already known protein, the sequence is kept. Examples of such cloned full-length cDNAs containing sequences of interest are described in Example 21. Sequences resulting from chimera or double inserts or located on chromosome breaking points as assessed by homology to other sequences may be 20 discarded during this procedure.

Extended cDNAs prepared as described above may be subsequently engineered to obtain nucleic acids which include desired portions of the extended cDNA using conventional techniques such as subcloning, PCR, or in vitro oligonucleotide synthesis. For example, nucleic acids which include only the full coding sequences may be obtained using techniques known to those skilled in the art.

25 Alternatively, conventional techniques may be applied to obtain nucleic acids which contain only part of the coding sequences. In the case of nucleic acids encoding secreted proteins, nucleic acids containing only the coding sequence for the mature protein remaining after the signal peptide is cleaved off or nucleic acids which contain only the coding sequences for the signal peptides may be obtained.

Similarly, nucleic acids containing any other desired portion of the coding sequences for the 30 encoded protein may be obtained. For example, the nucleic acid may contain at least 10, 15, 18, 20, 25, 28, 30, 35, 40, 50, 75, 100, 150, 200, 300, 400 or 500 consecutive bases of an extended cDNA.

Once an extended cDNA has been obtained, it can be sequenced to determine the amino acid sequence it encodes. Once the encoded amino acid sequence has been determined, one can create and identify any of the many conceivable cDNAs that will encode that protein by simply using the 35 degeneracy of the genetic code. For example, allelic variants or other homologous nucleic acids can be identified as described below. Alternatively, nucleic acids encoding the desired amino acid sequence can be synthesized in vitro.

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In a preferred embodiment, the coding sequence may be selected using the known codon or codon pair preferences for the host organism in which the cDNA is to be expressed.

In addition to PCR based methods for obtaining cDNAs which include the authentic 5'end of the corresponding mRNA as well as the complete protein coding sequence of the corresponding mRNA, traditional hybridization based methods may also be employed. These methods may also be used to obtain the genomic DNAs which encode the mRNAs from which the 5' ESTs or consensus contigated 5' ESTS were derived, mRNAs corresponding to the extended cDNAs, or nucleic acids which are homologous to extended cDNAs, 5' ESTs, or consensus contigated 5' ESTs. Example 19 below provides examples of such methods.

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EXAMPLE 20

Methods for Obtaining Extended cDNAs which Include the Entire Coding Region and the Authentic 5'End of the Corresponding mRNA or Nucleic Acids Homologous to Extended cDNAs, 5' ESTs or Consensus Contigated 5' ESTs

A full-length cDNA library can be made using the strategies described in Example 7.

Alternatively, a cDNA library or genomic DNA library may be obtained from a commercial source or made using techniques familiar to those skilled in the art.

Such cDNA or genomic DNA libraries may be used to isolate extended cDNAs obtained from 5' ESTs or consensus contigated 5' ESTs or nucleic acids homologous to extended cDNAs, 5' ESTs, or consensus contigated 5' ESTs as follows. The cDNA library or genomic DNA library is hybridized to a detectable probe. The detectable probe may comprise at least 10, 15, 18, 20, 25, 28, 30, 35, 40, 50, 75, 100, 150, 200, 300, 400 or 500 consecutive nucleotides of the 5' EST, consensus contigated 5' EST, or extended cDNA.

Techniques for identifying cDNA clones in a cDNA library which hybridize to a given probe

sequence are disclosed in Sambrook et al., Molecular Cloning: A Laboratory Manual 2d Ed., Cold

Spring Harbor Laboratory Press, 1989. The same techniques may be used to isolate genomic DNAs.

Briefly, cDNA or genomic DNA clones which hybridize to the detectable probe are identified and isolated for further manipulation as follows. The detectable probe described in the preceding paragraph is labeled with a detectable label such as a radioisotope or a fluorescent molecule. Techniques for

labeling the probe are well known and include phosphorylation with polynucleotide kinase, nick translation, in vitro transcription, and non radioactive techniques. The cDNAs or genomic DNAs in the library are transferred to a nitrocellulose or nylon filter and denatured. After blocking of non specific sites, the filter is incubated with the labeled probe for an amount of time sufficient to allow binding of the probe to cDNAs or genomic DNAs containing a sequence capable of hybridizing thereto.

By varying the stringency of the hybridization conditions used to identify cDNAs or genomic DNAs which hybridize to the detectable probe, cDNAs or genomic DNAs having different levels of homology to the probe can be identified and isolated as described below.

1. Identification of cDNA or Genomic DNA Sequences Having a High Degree of Homology to the Labeled Probe

To identify cDNAs or genomic DNAs having a high degree of homology to the probe sequence, the melting temperature of the probe may be calculated using the following formulas:

For probes between 14 and 70 nucleotides in length the melting temperature (Tm) is calculated using the formula: Tm=81.5+16.6(log (Na+))+0.41(fraction G+C)-(600/N) where N is the length of the probe.

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If the hybridization is carried out in a solution containing formamide, the melting temperature may be calculated using the equation Tm=81.5+16.6(log (Na+))+0.41(fraction G+C)-(0.63% formamide)-(600/N) where N is the length of the probe.

Prehybridization may be carried out in 6X SSC, 5X Denhardt's reagent, 0.5% SDS, 100 μg denatured fragmented salmon sperm DNA or 6X SSC, 5X Denhardt's reagent, 0.5% SDS, 100 μg denatured fragmented salmon sperm DNA, 50% formamide. The formulas for SSC and Denhardt's solutions are listed in Sambrook *et al.*, *supra*.

Hybridization is conducted by adding the detectable probe to the prehybridization solutions listed above. Where the probe comprises double stranded DNA, it is denatured before addition to the hybridization solution. The filter is contacted with the hybridization solution for a sufficient period of time to allow the probe to hybridize to extended cDNAs or genomic DNAs containing sequences complementary thereto or homologous thereto. For probes over 200 nucleotides in length, the hybridization may be carried out at 15-25°C below the Tm. For shorter probes, such as oligonucleotide probes, the hybridization may be conducted at 15-25°C below the Tm. Preferably, for hybridizations in 6X SSC, the hybridization is conducted at approximately 68°C. Preferably, for hybridizations in 50% formamide containing solutions, the hybridization is conducted at approximately 42°C.

All of the foregoing hybridizations would be considered to be under "stringent" conditions.

Following hybridization, the filter is washed in 2X SSC, 0.1% SDS at room temperature for 15 minutes. The filter is then washed with 0.1X SSC, 0.5% SDS at room temperature for 30 minutes to 1 hour. Thereafter, the solution is washed at the hybridization temperature in 0.1X SSC, 0.5% SDS. A final wash is conducted in 0.1X SSC at room temperature.

cDNAs or genomic DNAs which have hybridized to the probe are identified by autoradiography or other conventional techniques.

2. Obtaining cDNA or Genomic DNA Sequences Having Lower Degrees of Homology to the Labeled Probe

The above procedure may be modified to identify cDNAs or genomic DNAs having decreasing levels of homology to the probe sequence. For example, to obtain cDNAs or genomic DNAs of decreasing homology to the detectable probe, less stringent conditions may be used. For example, the hybridization temperature may be decreased in increments of 5°C from 68°C to 42°C in a hybridization buffer having a sodium concentration of approximately 1M. Following hybridization, the filter may be

washed with 2X SSC, 0.5% SDS at the temperature of hybridization. These conditions are considered to be "moderate" conditions above 50°C and "low" conditions below 50°C.

Alternatively, the hybridization may be carried out in buffers, such as 6X SSC, containing formamide at a temperature of 42°C. In this case, the concentration of formamide in the hybridization buffer may be reduced in 5% increments from 50% to 0% to identify clones having decreasing levels of homology to the probe. Following hybridization, the filter may be washed with 6X SSC, 0.5% SDS at 50°C. These conditions are considered to be "moderate" conditions above 25% formamide and "low" conditions below 25% formamide. cDNAs or genomic DNAs which have hybridized to the probe are identified by autoradiography.

3. Determination of the Degree of Homology between the Obtained cDNAs or Genomic DNAs and 5'ESTs, Consensus Contigated 5'ESTs, or Extended cDNAs or Between the Polypeptides Encoded by the Obtained cDNAs or Genomic DNAs and the Polypeptides Encoded by the 5'ESTs, Consensus Contigated 5'ESTs, or Extended cDNAs

To determine the level of homology between the hybridized cDNA or genomic DNA and the 5'EST, consensus contigated 5'EST or extended cDNA from which the probe was derived, the nucleotide sequences of the hybridized nucleic acid and the 5'EST, consensus contigated 5'EST or extended cDNA from which the probe was derived are compared. The sequences of the 5'EST, consensus contigated 5'EST or extended cDNA from which the probe was derived and the sequences of the cDNA or genomic DNA which hybridized to the detectable probe may be stored on a computer readable medium as described below and compared to one another using any of a variety of algorithms familiar to those skilled in the art, those described below.

To determine the level of homology between the polypeptide encoded by the hybridizing cDNA or genomic DNA and the polypeptide encoded by the 5'EST, consensus contigated 5'EST or extended cDNA from which the probe was derived, the polypeptide sequence encoded by the hybridized nucleic acid and the polypeptide sequence encoded by the 5'EST, consensus contigated 5'EST or extended cDNA from which the probe was derived are compared. The sequences of the polypeptide encoded by the 5'EST, consensus contigated 5'EST or extended cDNA from which the probe was derived and the polypeptide sequence encoded by the cDNA or genomic DNA which hybridized to the detectable probe may be stored on a computer readable medium as described below and compared to one another using any of a variety of algorithms familiar to those skilled in the art, those described below.

Protein and/or nucleic acid sequence homologies may be evaluated using any of the variety of sequence comparison algorithms and programs known in the art. Such algorithms and programs include, but are by no means limited to, TBLASTN, BLASTP, FASTA, TFASTA, and CLUSTALW (Pearson and Lipman, 1988, Proc. Natl. Acad. Sci. USA 85(8):2444-2448; Altschul et al., 1990, J. Mol. Biol. 215(3):403-410; Thompson et al., 1994, Nucleic Acids Res. 22(2):4673-4680; Higgins et al., 1996, Methods Enzymol. 266:383-402; Altschul et al., 1990, J. Mol. Biol. 215(3):403-410; Altschul et al., 1993, Nature Genetics 3:266-272).

In a particularly preferred embodiment, protein and nucleic acid sequence homologies are evaluated using the Basic Local Alignment Search Tool ("BLAST") which is well known in the art (see, e.g., Karlin and Altschul, 1990, Proc. Natl. Acad. Sci. USA 87:2267-2268; Altschul et al., 1990, J. Mol. Biol. 215:403-410; Altschul et al., 1993, Nature Genetics 3:266-272; Altschul et al., 1997, Nuc. Acids Res. 25:3389-3402). In particular, five specific BLAST programs are used to perform the

- (1) BLASTP and BLAST3 compare an amino acid query sequence against a protein sequence database;
- (2) BLASTN compares a nucleotide query sequence against a nucleotide sequence 10 database;

following task:

- (3) BLASTX compares the six-frame conceptual translation products of a query nucleotide sequence (both strands) against a protein sequence database;
- (4) TBLASTN compares a query protein sequence against a nucleotide sequence database translated in all six reading frames (both strands); and
- 15 (5) TBLASTX compares the six-frame translations of a nucleotide query sequence against the six-frame translations of a nucleotide sequence database.

The BLAST programs identify homologous sequences by identifying similar segments, which are referred to herein as "high-scoring segment pairs," between a query amino or nucleic acid sequence and a test sequence which is preferably obtained from a protein or nucleic acid sequence database. High-scoring segment pairs are preferably identified (i.e., aligned) by means of a scoring matrix, many of which are known in the art. Preferably, the scoring matrix used is the BLOSUM62 matrix (Gonnet et al., 1992, Science 256:1443-1445; Henikoff and Henikoff, 1993, Proteins 17:49-61). Less preferably, the PAM or PAM250 matrices may also be used (see, e.g., Schwartz and Dayhoff, eds., 1978, Matrices for Detecting Distance Relationships: Atlas of Protein Sequence and 25 Structure, Washington: National Biomedical Research Foundation)

The BLAST programs evaluate the statistical significance of all high-scoring segment pairs identified, and preferably selects those segments which satisfy a user-specified threshold of significance, such as a user-specified percent homology. Preferably, the statistical significance of a high-scoring segment pair is evaluated using the statistical significance formula of Karlin (see, e.g., Karlin and Altschul, 1990, Proc. Natl. Acad. Sci. USA 87:2267-2268).

The parameters used with the above algorithms may be adapted depending on the sequence length and degree of homology studied. In some embodiments, the parameters may be the default parameters used by the algorithms in the absence of instructions from the user.

In some embodiments, the level of homology between the hybridized nucleic acid and the extended cDNA, 5'EST, or 5' consensus contigated 5'EST from which the probe was derived may be determined using the FASTDB algorithm described in Brutlag *et al.* Comp. App. Biosci. 6:237-245, 1990. In such analyses the parameters may be selected as follows: Matrix=Unitary, k-tuple=4,

Mismatch Penalty=1, Joining Penalty=30, Randomization Group Length=0, Cutoff Score=1, Gap Penalty=5, Gap Size Penalty=0.05, Window Size=500 or the length of the sequence which hybridizes to the probe, whichever is shorter. Because the FASTDB program does not consider 5' or 3' truncations when calculating homology levels, if the sequence which hybridizes to the probe is truncated relative to 5 the sequence of the extended cDNA, 5'EST, or consensus contigated 5'EST from which the probe was derived the homology level is manually adjusted by calculating the number of nucleotides of the extended cDNA, 5'EST, or consensus contigated 5' EST which are not matched or aligned with the hybridizing sequence, determining the percentage of total nucleotides of the hybridizing sequence which the non-matched or non-aligned nucleotides represent, and subtracting this percentage from the 10 homology level. For example, if the hybridizing sequence is 700 nucleotides in length and the extended cDNA, 5'EST, or consensus contigated 5' EST sequence is 1000 nucleotides in length wherein the first 300 bases at the 5' □end of the extended cDNA, 5'EST, or consensus contigated 5' EST are absent from the hybridizing sequence, and wherein the overlapping 700 nucleotides are identical, the homology level would be adjusted as follows. The non-matched, non-aligned 300 bases represent 30% of the length of 15 the extended cDN 4, 5'EST, or consensus contigated 5' EST. If the overlapping 700 nucleotides are 100% identical, the adjusted homology level would be 100-30=70% homology. It should be noted that the preceding adjustments are only made when the non-matched or non-aligned nucleotides are at the 5'or 3'ends. No adjustments are made if the non-matched or non-aligned sequences are internal or under any other conditions.

For example, using the above methods, nucleic acids having at least 95% nucleic acid homology, at least 96% nucleic acid homology, at least 97% nucleic acid homology, at least 98% nucleic acid homology, at least 99% nucleic acid homology, or more than 99% nucleic acid homology to the extended cDNA, 5'EST, or consensus contigated 5' EST from which the probe was derived may be obtained and identified. Such nucleic acids may be allelic variants or related nucleic acids from other 25 species. Similarly, by using progressively less stringent hybridization conditions one can obtain and identify nucleic acids having at least 90%, at least 85%, at least 80% or at least 75% homology to the extended cDNA, 5'EST, or consensus contigated 5' EST from which the probe was derived.

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Using the above methods and algorithms such as FASTA with parameters depending on the sequence length and degree of homology studied, for example the default parameters used by the 30 algorithms in the absence of instructions from the user, one can obtain nucleic acids encoding proteins having at least 99%, at least 98%, at least 97%, at least 96%, at least 95%, at least 90%, at least 85%, at least 80% or at least 75% homology to the protein encoded by the extended cDNA, 5'EST, or consensus contigated 5' EST from which the probe was derived. In some embodiments, the homology levels can be determined using the "default" opening penalty and the "default" gap penalty, and a scoring matrix 35 such as PAM 250 (a standard scoring matrix; see Dayhoff et al., in: Atlas of Protein Sequence and Structure, Vol. 5, Supp. 3 (1978)).

Alternatively, the level of polypeptide homology may be determined using the FASTDB algorithm described by Brutlag et al. Comp. App. Biosci. 6:237-245, 1990. In such analyses the parameters may be selected as follows: Matrix=PAM 0, k-tuple=2, Mismatch Penalty=1, Joining Penalty=20, Randomization Group Length=0, Cutoff Score=1, Window Size=Sequence Length, Gap 5 Penalty=5, Gap Size Penalty=0.05, Window Size=500 or the length of the homologous sequence. whichever is shorter. If the homologous amino acid sequence is shorter than the amino acid sequence encoded by the extended cDNA, 5'EST, or consensus contigated 5' EST as a result of an N terminal and/or C terminal deletion the results may be manually corrected as follows. First, the number of amino acid residues of the amino acid sequence encoded by the extended cDNA, 5'EST, or consensus 10 contigated 5' EST which are not matched or aligned with the homologous sequence is determined. Then, the percentage of the length of the sequence encoded by the extended cDNA, 5'EST, or consensus contigated 5' EST which the non-matched or non-aligned amino acids represent is calculated. This percentage is subtracted from the homology level. For example wherein the amino acid sequence encoded by the extended cDNA, 5'EST, or consensus contigated 5' EST is 100 amino acids in length 15 and the length of the homologous sequence is 80 amino acids and wherein the amino acid sequence encoded by the extended cDNA or 5'EST is truncated at the N terminal end with respect to the homologous sequence, the homology level is calculated as follows. In the preceding scenario there are 20 non-matched, non-aligned amino acids in the sequence encoded by the extended cDNA, 5'EST, or consensus contigated 5' EST. This represents 20% of the length of the amino acid sequence encoded by 20 the extended cDNA, 5'EST, or consensus contigated 5' EST. If the remaining amino acids are 1005 identical between the two sequences, the homology level would be 100%-20%=80% homology. No adjustments are made if the non-matched or non-aligned sequences are internal or under any other conditions.

In addition to the above described methods, other protocols are available to obtain extended cDNAs using 5' ESTs or consensus contigated 5'ESTs as outlined in the following paragraphs.

Extended cDNAs may be prepared by obtaining mRNA from the tissue, cell, or organism of interest using mRNA preparation procedures utilizing polyA selection procedures or other techniques known to those skilled in the art. A first primer capable of hybridizing to the polyA tail of the mRNA is hybridized to the mRNA and a reverse transcription reaction is performed to generate a first cDNA strand.

The first cDNA strand is hybridized to a second primer containing at least 10 consecutive nucleotides of the sequences of SEQ ID NOs 24-811 and 1600-1622. Preferably, the primer comprises at least 10, 12, 15, 17, 18, 20, 23, 25, or 28 consecutive nucleotides from the sequences of SEQ ID NOs 24-811 and 1600-1622. In some embodiments, the primer comprises more than 30 nucleotides from the sequences of SEQ ID NOs 24-811 and 1600-1622. If it is desired to obtain extended cDNAs containing the full protein coding sequence, including the authentic translation initiation site, the second primer used contains sequences located upstream of the translation initiation site. The second primer is

extended to generate a second cDNA strand complementary to the first cDNA strand. Alternatively, RT-PCR may be performed as described above using primers from both ends of the cDNA to be obtained.

Extended cDNAs containing 5' fragments of the mRNA may be prepared by hybridizing an mRNA comprising the sequences of SEQ ID NOs. 24-811 and 1600-1622 with a primer comprising a 5 complementary to a fragment of an EST-related nucleic acid hybridizing the primer to the mRNAs, and reverse transcribing the hybridized primer to make a first cDNA strand from the mRNAs. Preferably, the primer comprises at least 10, 12, 15, 17, 18, 20, 23, 25, or 28 consecutive nucleotides of the sequences complementary to SEQ ID NOs. 24-811 and 1600-1622.

Thereafter, a second cDNA strand complementary to the first cDNA strand is synthesized. The 10 second cDNA strand may be made by hybridizing a primer complementary to sequences in the first cDNA strand to the first cDNA strand and extending the primer to generate the second cDNA strand.

The double stranded extended cDNAs made using the methods described above are isolated and cloned. The extended cDNAs may be cloned into vectors such as plasmids or viral vectors capable of replicating in an appropriate host cell. For example, the host cell may be a bacterial, mammalian, 15 avian, or insect cell.

Techniques for isolating mRNA, reverse transcribing a primer hybridized to mRNA to generate a first cDNA strand, extending a primer to make a second cDNA strand complementary to the first cDNA strand, isolating the double stranded cDNA and cloning the double stranded cDNA are well known to those skilled in the art and are described in Current Protocols in Molecular Biology, John 20 Wiley & Sons, Inc. 1997 and Sambrook et al., Molecular Cloning: A Laboratory Manual, Second Edition, Cold Spring Harbor Laboratory Press, 1989.

Alternatively, other procedures may be used for obtaining full-length cDNAs or extended cDNAs. In one approach, full-length or extended cDNAs are prepared from mRNA and cloned into double stranded phagemids as follows. The cDNA library in the double stranded phagemids is then 25 rendered single stranded by treatment with an endonuclease, such as the Gene II product of the phage F1 and an exonuclease (Chang et al., Gene 127:95-8, 1993). A biotinylated oligonucleotide comprising the sequence of a fragment of an EST-related nucleic acid is hybridized to the single stranded phagemids. Preferably, the fragment comprises at least 10, 12, 15, 17, 18, 20, 23, 25, or 28 consecutive nucleotides of the sequences of SEQ ID NOs. 24-811 and 1600-1622.

Hybrids between the biotinylated oligonucleotide and phagemids are isolated by incubating the hybrids with streptavidin coated paramagnetic beads and retrieving the beads with a magnet (Fry et al., Biotechniques, 13: 124-131, 1992). Thereafter, the resulting phagemids are released from the beads and converted into double stranded DNA using a primer specific for the 5' EST or consensus contigated 5'EST sequence used to design the biotinylated oligonucleotide. Alternatively, protocols such as the 35 Gene Trapper kit (Gibco BRL) may be used. The resulting double stranded DNA is transformed into bacteria. Extended cDNAs or full length cDNAs containing the 5' EST or consensus contigated 5'EST sequence are identified by colony PCR or colony hybridization.

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Using any of the above described methods in section III, a plurality of extended cDNAs containing full-length protein coding sequences or portions of the protein coding sequences may be provided as cDNA libraries for subsequent evaluation of the encoded proteins or use in diagnostic assays as described below.

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EXAMPLE 21

Full Length cDNAs

The procedures described in Example 19 and 20 were used to obtain extended cDNAs or full length cDNAs derived from 5' ESTs in a variety of tissues. The following list provides a few examples 10 of cDNAs obtained by these means.

Using this procedure, the full length cDNA of SEQ ID NO:1 (internal identification number 58-34-2-E7-FL2) was obtained. This cDNA encodes the signal peptide MWWFQQGLSFLPSALVIWTSA (SEQ ID NO:2) having a von Heijne score of 5.5.

Using this approach, the full length cDNA of SEQ ID NO:3 (internal identification number 48-15 19-3-G1-FL1) was obtained. This cDNA encodes the signal peptide MKKVLLLITAILAVAVG (SEQ ID NO: 4) having a von Heijne score of 8.2.

The full length cDNA of SEQ ID NO:5 (internal identification number 58-35-2-F10-FL2) was also obtained using this procedure. This cDNA encodes a signal peptide LWLLFFLVTAIHA (SEQ ID NO:6) having a von Heijne score of 10.7.

Furthermore, the polypeptides encoded by the extended or full-length cDNAs may be screened for the presence of known structural or functional motifs or for the presence of signatures, small amino acid sequences which are well conserved amongst the members of a protein family. The results obtained for the polypeptides encoded by a few full-length cDNAs derived from 5'ESTs that were screened for the presence of known protein signatures and motifs using the Proscan software from the GCG package and the Prosite 15.0 database are provided below.

The protein of SEQ ID NO: 8 encoded by the full-length cDNA SEQ ID NO: 7 (internal designation 78-8-3-E6-CL0_1C) and expressed in adult prostate belong to the phosphatidylethanolamine-binding protein from which it exhibits the characteristic PROSITE signature from positions 90 to 112. Proteins from this widespread family, from nematodes to fly, yeast, rodent and primate species, bind hydrophobic ligands such as phospholipids and nucleotides. They are mostly expressed in brain and in testis and are thought to play a role in cell growth and/or maturation, in regulation of the sperm maturation, motility and in membrane remodeling. They may act either through signal transduction or through oxidoreduction reactions (for a review see Schoentgen and Jollès, *FEBS Letters*, 369:22-26 (1995)). Taken together, these data suggest that the protein of SEQ ID NO: 8 may play a role in cell growth, maturation and in membrane remodeling and/or may be related to male fertility. Thus, these protein may be useful in diagnosing and/or treating cancer, neurodegenerative diseases, and/or disorders related to male fertility and sterility.

The protein of SEQ ID No. 10 encoded by the full-length cDNA SEQ ID No. 9 (internal designation 108-013-5-O-H9-FLC) shows homologies with a family of lysophospholipases conserved among eukaryotes (yeast, rabbit, rodents and human). In addition, some members of this family exhibit a calcium-independent phospholipase A2 activity (Portilla et al, J. Am. Soc. Nephro., 9:1178-1186 (1998)). All members of this family exhibit the active site consensus GXSXG motif of carboxylesterases that is also found in the protein of SEQ ID No. 10 (position 54 to 58). In addition, this protein may be a membrane protein with one transmembrane domain as predicted by the software TopPred II (Claros and von Heijne, CABIOS applic. Notes, 10:685-686 (1994)). Taken together, these data suggest that the protein of SEQ ID NO:10 may play a role in fatty acid metabolism, probably as a phospholipase. Thus, this protein or part therein, may be useful in diagnosing and/or treating several disorders including, but not limited to, cancer, diabetes, and neurodegenerative disorders such as Parkinson's and Alzheimer's diseases. It may also be useful in modulating inflammatory responses to infectious agents and/or to suppress graft rejection.

The protein of SEQ ID NO: 12 encoded by the full-length cDNA SEQ ID NO: 11 (internal 15 designation 108-004-5-0-D10-FLC) shows remote homology to a subfamily of beta4galactosyltransferases widely conserved in animals (human, rodents, cow and chicken). Such enzymes, usually type II membrane proteins located in the endoplasmic reticulum or in the Golgi apparatus, catalyzes the biosynthesis of glycoproteins, glycolipid glycans and lactose. Their characteristic features defined as those of subfamily A in Breton et al, J. Biochem., 123:1000-1009 20 (1998) are pretty well conserved in the protein of SEQ ID NO: 12, especially the region I containing the DVD motif (positions 163-165) thought to be involved either in UDP binding or in the catalytic process itself. In addition, the protein of SEQ ID NO: 12 has the typical structure of a type II protein. Indeed, it contains a short 28-amino-acid-long N-terminal tail, a transmembrane segment from positions 29 to 49 and a large 278-amino-acid-long C-terminal tail as predicted by the software 25 TopPred II (Claros and von Heijne, CABIOS applic. Notes, 10:685-686 (1994)). Taken together, these data suggest that the protein of SEQ ID NO: 12 may play a role in the biosynthesis of polysaccharides, and of the carbohydrate moieties of glycoproteins and glycolipids and/or in cell-cell recognition. Thus, this protein may be useful in diagnosing and/or treating several types of disorders including, but not limited to, cancer, atherosclerosis, cardiovascular disorders, autoimmune disorders 30 and rheumatic diseases including rheumatoid arthritis.

The protein of SEQ ID NO: 14 encoded by the full-length cDNA SEQ ID NO: 13 (internal designation 108-009-5-0-A2-FLC) shows extensive homology to the bZIP family of transcription factors, and especially to the human luman protein (Lu et al., Mol. Cell. Biol., 17:5117-5126 (1997))). The match include the whole bZIP domain composed of a basic DNA-binding domain and of a leucine zipper allowing protein dimerization. The basic domain is conserved in the protein of SEQ ID NO: 14 as shown by the characteristic PROSITE signature (positions 224-237) except for a conservative substitution of a glutamic acid with an aspartic acid in position 233. The typical

PROSITE signature for leucine zipper is also present (positions 259 to 280). Taken together, these data suggest that the protein of SEQ ID NO: 14 may bind to DNA, hence regulating gene expression as a transcription factor. Thus, this protein may be useful in diagnosing and/or treating several types

Bacterial clones containing plasmids containing the full length cDNAs described above are presently stored in the inventor's laboratories under the internal identification numbers provided above. The inserts may be recovered from the deposited materials by growing an aliquot of the appropriate bacterial clone in the appropriate medium. The plasmid DNA can then be isolated using plasmid isolation procedures familiar to those skilled in the art such as alkaline lysis minipreps or large scale alkaline lysis plasmid isolation procedures. If desired the plasmid DNA may be further enriched by centrifugation on a cesium chloride gradient, size exclusion chromatography, or anion exchange

chromatography. The plasmid DNA obtained using these procedures may then be manipulated using standard cloning techniques familiar to those skilled in the art. Alternatively, a PCR can be done with primers designed at both ends of the insertion. The PCR product which corresponds to the cDNA insert

15 can then be manipulated using standard cloning techniques familiar to those skilled in the art.

V. Expression of Proteins or Polypeptides Encoded by EST-related nucleic acids or Fragments thereof

EST-related nucleic acids, fragments of EST-related nucleic acids, positional segments of EST20 related nucleic acids, and fragments of positional segments of EST-related nucleic acids may be used to
express the polypeptides which they encode. In particular, they may be used to express EST-related
polypeptides, fragments of EST-related polypeptides, positional segments of EST-related polypeptides,
or fragments of positional segments of EST-related polypeptides. In some embodiments, the ESTrelated nucleic acids, positional segments of EST-related nucleic acids, and fragments of positional
25 segments of EST-related nucleic acids may be used to express the full polypeptide (*i.e.* the signal peptide
and the mature polypeptide) of a secreted protein, the mature protein (*i.e.* the polypeptide generated after
cleavage of the signal peptide), or the signal peptide of a secreted protein. If desired, nucleic acids
encoding the signal peptide may be used to facilitate secretion of the expressed protein. It will be
appreciated that a plurality of EST-related nucleic acids, fragments of EST-related nucleic acids,
30 positional segments of EST-related nucleic acids, or fragments of positional segments of EST-related
nucleic acids may be simultaneously cloned into expression vectors to create an expression library for
analysis of the encoded proteins as described below.

EXAMPLE 22

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To express their encoded proteins, the EST-related nucleic acids, fragments of EST-related nucleic acids, positional segments of EST-related nucleic acids, or fragments of positional segments of EST-related nucleic acids are cloned into a suitable expression vector. In some instances, nucleic acids encoding EST-related polypeptides, fragments of EST-related polypeptides, positional segments of EST-related polypeptides or fragments of positional segments of EST-related polypeptides may be cloned into a suitable expression vector.

In some embodiments, the nucleic acids inserted into the expression vector may comprise the coding sequence of a sequence selected from the group consisting of SEQ ID NOs. 24-811. In other embodiments, the nucleic acids inserted into the expression vector may comprise may comprise the full coding sequence (*i.e.* the nucleotides encoding the signal peptide and the mature polypeptide) of one of SEQ ID Nos. 766-792. In some embodiments, the nucleic acid inserted into the expression vector may comprise the nucleotides of one of the sequences of SEQ ID Nos. 766-792 which encode the mature polypeptide (*i.e.* the nucleotides encoding the polypeptide generated after cleavage of the signal peptide). In further embodiments, the nucleic acids inserted into the expression vector may comprise the nucleotides of 24-728 and 766-792 which encode the signal peptide to facilitate secretion of the expressed protein. The nucleic acids inserted into the expression vectors may also contain sequences upstream of the sequences encoding the signal peptide, such as sequences which regulate expression levels or sequences which confer tissue specific expression.

The nucleic acid inserted into the expression vector may encode a polypeptide comprising the
one of the sequences of SEQ ID Nos. 812-1599. In some embodiments, the nucleic acid inserted into
the expression vector may encode the full polypeptide sequence (*i.e.* the signal peptide and the mature
polypeptide) included in one of SEQ ID Nos. 1554-1580. In other embodiments, the nucleic acid
inserted into the expression vector may encode the mature polypeptide (*i.e.* the polypeptide generated
after cleavage of the signal peptide) included in one of the sequences of SEQ ID Nos. 1554-1580. In
further embodiments, the nucleic acids inserted into the expression vector may encode the signal peptide
included in one of the sequences of 812-1516 and 1554-1580.

The nucleic acid encoding the protein or polypeptide to be expressed is operably linked to a promoter in an expression vector using conventional cloning technology. The expression vector may be any of the mammalian, yeast, insect or bacterial expression systems known in the art. Commercially available vectors and expression systems are available from a variety of suppliers including Genetics Institute (Cambridge, MA), Stratagene (La Jolla, California), Promega (Madison, Wisconsin), and Invitrogen (San Diego, California). If desired, to enhance expression and facilitate proper protein folding, the codon context and codon pairing of the sequence may be optimized for the particular expression organism in which the expression vector is introduced, as explained by Hatfield, *et al.*, U.S. Patent No. 5,082,767.

The following is provided as one exemplary method to express the proteins encoded by the nucleic acids described above. In some instances the nucleic acid encoding the protein or polypeptide to

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be expressed includes a methionine initiation codon and a polyA signal. If the nucleic acid encoding the polypeptide to be expressed lacks a methionine to serve as the initiation site, an initiating methionine can be introduced next to the first codon of the nucleic acid using conventional techniques. Similarly, if the nucleic acid encoding the protein or polypeptide to be expressed lacks a polyA signal, this sequence can 5 be added to the construct by, for example, splicing out the polyA signal from pSG5 (Stratagene) using Bgll and Sall restriction endonuclease enzymes and incorporating it into the mammalian expression vector pXT1 (Stratagene). pXT1 contains the LTRs and a portion of the gag gene from Moloney Murine Leukemia Virus. The position of the LTRs in the construct allow efficient stable transfection. The vector includes the Herpes Simplex thymidine kinase promoter and the selectable neomycin gene. 10 The nucleic acid encoding the polypeptide to be expressed is obtained by PCR from the bacterial vector using oligonucleotide primers complementary to the nucleic acid encoding the protein or polypeptide to be expressed and containing restriction endonuclease sequences for Pst I incorporated into the 5'primer and Bglll at the 5' end of 3' primer, taking care to ensure that the nucleic acid encoding the protein or polypeptide to be expressed is correctly positioned with respect to the poly A signal. The purified 15 fragment obtained from the resulting PCR reaction is digested with PstI, blunt ended with an exonuclease, digested with Bgl II, purified and ligated to pXT1, now containing a poly A signal and digested with BglII.

The ligated product is transfected into mouse NIH 3T3 cells using Lipofectin (Life Technologies, Inc., Grand Island, New York) under conditions outlined in the product specification.

20 Positive transfectants are selected after growing the transfected cells in 600 µg/ml G418 (Sigma, St. Louis, Missouri).

Alternatively, the nucleic acid encoding the protein or polypeptide to be expressed may be cloned into pED6dpc2. The resulting pED6dpc2 constructs may be transfected into a suitable host cell, such as COS 1 cells. Methotrexate resistant cells are selected and expanded. The expressed protein or polypeptide may be isolated, purified, or enriched as described above.

To confirm expression of the desired protein or polypeptide, the proteins or polypeptides produced by cells containing a vector with a nucleic acid insert encoding the protein or polypeptide are compared to those lacking such an insert. The expressed proteins are detected using techniques familiar to those skilled in the art such as Coomassie blue or silver staining or using antibodies against the protein or polypeptide encoded by the nucleic acid insert. Antibodies capable of specifically recognizing the protein of interest may be generated using synthetic 15-mer peptides having a sequence encoded by the appropriate nucleic acid. The synthetic peptides are injected into mice to generate antibody to the polypeptide encoded by the nucleic acid.

If the proteins or polypeptides encoded by the nucleic acid inserts are secreted, medium

35 prepared from the host cells or organisms containing an expression vector which contains a nucleic acid insert encoding the desired protein or polypeptide is compared to medium prepared from the control cells or organism. The presence of a band in medium from the cells containing the nucleic acid insert which

is absent from preparations from the control cells indicates that the protein or polypeptide encoded by the nucleic acid insert is being expressed and secreted. Generally, the band corresponding to the protein encoded by the nucleic acid insert will have a mobility near that expected based on the number of amino acids in the open reading frame of the nucleic acid insert. However, the band may have a mobility different than that expected as a result of modifications such as glycosylation, ubiquitination, or enzymatic cleavage.

Alternatively, if the protein expressed from the above expression vectors does not contain sequences directing its secretion, the proteins expressed from host cells containing an expression vector with an insert encoding a secreted protein or portion thereof can be compared to the proteins expressed in control host cells containing the expression vector without an insert. The presence of a band in samples from cells containing the expression vector with an insert which is absent in samples from cells containing the expression vector without an insert indicates that the desired protein or portion thereof is being expressed. Generally, the band will have the mobility expected for the secreted protein or portion thereof. However, the band may have a mobility different than that expected as a result of modifications such as glycosylation, ubiquitination, or enzymatic cleavage.

The expressed protein or polypeptide may be purified, isolated or enriched using a variety of methods. In some methods, the protein or polypeptide may be secreted into the culture medium via a native signal peptide or a heterologous signal peptide operably linked thereto. In some methods, the protein or polypeptide may be linked to a heterologous polypeptide which facilitates its isolation, purification, or enrichment such as a nickel binding polypeptide. The protein or polypeptide may also be obtained by gel electrophoresis, ion exchange chromatography, size chromatography, hplc, salt precipitation, immunoprecipitation, a combination of any of the preceding methods, or any of the isolation, purification, or enrichment techniques familiar to those skilled in the art.

The protein encoded by the nucleic acid insert may also be purified using standard
immunochromatography techniques using immunoaffinity chromatography with antibodies directed against the encoded protein or polypeptide as described in more detail below. If antibody production is not possible, the nucleic acid insert encoding the desired protein or polypeptide may be incorporated into expression vectors designed for use in purification schemes employing chimeric polypeptides. In such strategies, the coding sequence of the nucleic acid insert is ligated in frame with the gene encoding the other half of the chimera. The other half of the chimera may be β-globin or a nickel binding polypeptide. A chromatography matrix having antibody to β-globin or nickel attached thereto is then used to purify the chimeric protein. Protease cleavage sites may be engineered between the β-globin gene or the nickel binding polypeptide and the extended cDNA or portion thereof. Thus, the two polypeptides of the chimera may be separated from one another by protease digestion.

One useful expression vector for generating β -globin chimerics is pSG5 (Stratagene), which encodes rabbit β -globin. Intron II of the rabbit β -globin gene facilitates splicing of the expressed transcript, and the polyadenylation signal incorporated into the construct increases the level of

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expression. These techniques as described are well known to those skilled in the art of molecular biology. Standard methods are published in methods texts such as Davis et al., (Basic Methods in Molecular Biology, L.G. Davis, M.D. Dibner, and J.F. Battey, ed., Elsevier Press, NY, 1986) and many of the methods are available from Stratagene, Life Technologies, Inc., or Promega. Polypeptide may 5 additionally be produced from the construct using in vitro translation systems such as the In vitro ExpressTM Translation Kit (Stratagene).

Following expression and purification of the proteins or polypeptides encoded by the nucleic acid inserts, the purified proteins may be tested for the ability to bind to the surface of various cell types as described in Example 23 below. It will be appreciated that a plurality of proteins expressed from 10 these nucleic acid inserts may be included in a panel of proteins to be simultaneously evaluated for the activities specifically described below, as well as other biological roles for which assays for determining activity are available.

EXAMPLE 23

Analysis of Secreted Proteins to Determine Whether they Bind to the Cell Surface

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The EST-related nucleic acids, fragments of EST-related nucleic acids, positional segments of EST-related nucleic acids, fragments of positional segments of EST-related nucleic acids, nucleic acids encoding the EST-related polypeptides, nucleic acids encoding fragments of the EST-related polypeptides, nucleic acids encoding positional segments of EST-related polypeptides, or nucleic acids encoding fragments of positional segments of EST-related polypeptides are cloned into expression 20 vectors such as those described in Example 22. The encoded proteins or polypeptides are purified, isolated, or enriched as described above. Following purification, isolation, or enrichment, the proteins or polypeptides are labeled using techniques known to those skilled in the art. The labeled proteins or polypeptides are incubated with cells or cell lines derived from a variety of organs or tissues to allow the proteins to bind to any receptor present on the cell surface. Following the incubation, the cells are 25 washed to remove non-specifically bound proteins or polypeptides. The specifically bound labeled proteins or polypeptides are detected by autoradiography. Alternatively, unlabeled proteins or polypeptides may be incubated with the cells and detected with antibodies having a detectable label, such as a fluorescent molecule, attached thereto.

Specificity of cell surface binding may be analyzed by conducting a competition analysis in 30 which various amounts of unlabeled protein or polypeptide are incubated along with the labeled protein or polypeptide. The amount of labeled protein or polypeptide bound to the cell surface decreases as the amount of competitive unlabeled protein or polypeptide increases. As a control, various amounts of an unlabeled protein or polypeptide unrelated to the labeled protein or polypeptide is included in some binding reactions. The amount of labeled protein or polypeptide bound to the cell surface does not 35 decrease in binding reactions containing increasing amounts of unrelated unlabeled protein, indicating that the protein or polypeptide encoded by the nucleic acid binds specifically to the cell surface.

As discussed above, human proteins have been shown to have a number of important physiological effects and, consequently, represent a valuable therapeutic resource. The human proteins or polypeptides made as described above may be evaluated to determine their physiological activities as described below.

EXAMPLE 24

Assaying the Expressed Proteins or Polypeptides for Cytokine, Cell Proliferation or Cell Differentiation Activity

As discussed above, some human proteins act as cytokines or may affect cellular proliferation or 10 differentiation. Many protein factors discovered to date, including all known cytokines, have exhibited activity in one or more factor dependent cell proliferation assays, and hence the assays serve as a convenient confirmation of cytokine activity. The activity of a protein or polypeptide of the present invention is evidenced by any one of a number of routine factor dependent cell proliferation assays for cell lines including, without limitation, 32D, DA2, DA1G, T10, B9, B9/11, BaF3, MC9/G, M⁺ (preB 15 Mh, 2E8, RB5, DA1, 123, T1165, HT2, CTLL2, TF-1, Mo7c and CMK. The proteins or polypeptides prepared as described above may be evaluated for their ability to regulate T cell or thymocyte proliferation in assays such as those described above or in the following references: Current Protocols in Immunology, Ed. by J.E. Coligan et al., Greene Publishing Associates and Wiley-Interscience; Takai et al. J. Immunol. 137:3494-3500, 1986., Bertagnolli et al. J. Immunol. 145:1706-1712, 1990., 20 Bertagnolli et al., Cellular Immunology 133:327-341, 1991. Bertagnolli, et al. J. Immunol. 149:3778-

3783, 1992; Bowman et al., J. Immunol. 152:1756-1761, 1994.

In addition, numerous assays for cytokine production and/or the proliferation of spleen cells, lymph node cells and thymocytes are known. These include the techniques disclosed in Current Protocols in Immunology. J.E. Coligan et al. Eds., 1:3.12.1-3.12.14, John Wiley and Sons, Toronto.

25 1994; and Schreiber, R.D. In Current Protocols in Immunology., supra 1: 6.8.1-6.8.8.

The proteins or polypeptides prepared as described above may also be assayed for the ability to regulate the proliferation and differentiation of hematopoietic or lymphopoietic cells. Many assays for such activity are familiar to those skilled in the art, including the assays in the following references: Bottomly et al., In Current Protocols in Immunology., supra. 1: 6.3.1-6.3.12,; deVries et al., J. Exp. 30 Med. 173:1205-1211, 1991; Moreau et al., Nature 36:690-692, 1988; Greenberger et al., Proc. Natl. Acad. Sci. U.S.A. 80:2931-2938, 1983; Nordan, R., In Current Protocols in Immunology., supra. 1: 6.6.1-6.6.5; Smith et al., Proc. Natl. Acad. Sci. U.S.A. 83:1857-1861, 1986; Bennett et al in Current Protocols in Immunology supra 1:6.15.1; Ciarletta et al In Current Protocols in Immunology. supra 1: 6.13.1.

The proteins or polypeptides prepared as described above may also be assayed for their ability to 35 regulate T-cell responses to antigens. Many assays for such activity are familiar to those skilled in the art, including the assays described in the following references: Chapter 3 (In vitro Assays for Mouse

Lymphocyte Function), Chapter 6 (Cytokines and Their Cellular Receptors) and Chapter 7, (Immunologic Studies in Humans) in Current Protocols in Immunology supra; Weinberger et al., Proc. Natl. Acad. Sci. USA 77:6091-6095, 1980; Weinberger et al., Eur. J. Immun. 11:405-411, 1981; Takai et al., J. Immunol. 137:3494-3500, 1986; Takai et al., J. Immunol. 140:508-512, 1988.

Those proteins or polypeptides which exhibit cytokine, cell proliferation, or cell differentiation activity may then be formulated as pharmaceuticals and used to treat clinical conditions in which induction of cell proliferation or differentiation is beneficial. Alternatively, as described in more detail below, nucleic acids encoding these proteins or polypeptides or nucleic acids regulating the expression of these proteins or polypeptides may be introduced into appropriate host cells to increase or decrease the expression of the proteins or polypeptides as desired.

EXAMPLE 25

Assaying the Expressed Proteins or Polypeptides for Activity as Immune System Regulators

The proteins or polypeptides prepared as described above may also be evaluated for their effects as immune regulators. For example, the proteins or polypeptides may be evaluated for their activity to influence thymocyte or splenocyte cytotoxicity. Numerous assays for such activity are familiar to those skilled in the art including the assays described in the following references: Chapter 3 (*In vitro* Assays for Mouse Lymphocyte Function 3.1-3.19) and Chapter 7 (Immunologic studies in Humans) in *Current Protocols in Immunology*, J.E. Coligan *et al.* Eds, Greene Publishing Associates and Wiley-Interscience; Herrmann *et al.*, *Proc. Natl. Acad. Sci. USA* 78:2488-2492, 1981; Herrmann *et al.*, *J. Immunol.* 128:1968-1974, 1982; Handa *et al.*, *J. Immunol.* 135:1564-1572, 1985; Takai *et al.*, *J. Immunol.* 137:3494-3500, 1986; Takai *et al.*, *J. Immunol.* 140:508-512, 1988; Bowman *et al.*, *J. Virology* 61:1992-1998; Bertagnolli *et al. Cell. Immunol.* 133:327-341, 1991; Brown *et al.*, *J. Immunol.* 153:3079-3092, 1994.

The proteins or polypeptides prepared as described above may also be evaluated for their effects on T-cell dependent immunoglobulin responses and isotype switching. Numerous assays for such activity are familiar to those skilled in the art, including the assays disclosed in the following references: Maliszewski, *J. Immunol.* 144:3028-3033, 1990; Mond *et al.* in *Current Protocols in Immunology*, 1: 3.8.1-3.8.16, *supra*.

The proteins or polypeptides prepared as described above may also be evaluated for their effect on immune effector cells, including their effect on Th1 cells and cytotoxic lymphocytes. Numerous assays for such activity are familiar to those skilled in the art, including the assays disclosed in the following references: Chapter 3 (*In vitro* Assays for Mouse Lymphocyte Function 3.1-3.19) and Chapter 7 (Immunologic Studies in Humans) in *Current Protocols in Immunology, supra*; Takai et al., J. Immunol. 137:3494-3500, 1986; Takai et al., J. Immunol. 140:508-512, 1988; Bertagnolli et al., J. Immunol. 149:3778-3783, 1992.

The proteins or polypeptides prepared as described above may also be evaluated for their effect on dendritic cell mediated activation of naive T-cells. Numerous assays for such activity are familiar to those skilled in the art, including the assays disclosed in the following references: Guery et al., J. Immunol. 134:536-544, 1995; Inaba et al., J. Exp. Med. 173:549-559, 1991; Macatonia et al., J. Simmunol. 154:5071-5079, 1995; Porgador et al J. Exp. Med 182:255-260, 1995; Nair et al., J. Virol. 67:4062-4069, 1993; Huang et al., Science 264:961-965, 1994; Macatonia et al J. Exp. Med 169:1255-1264, 1989; Bhardwaj et al., Journal of Clinical Investigation 94:797-807, 1994; and Inaba et al., J. Exp. Med 172:631-640, 1990.

The proteins or polypeptides prepared as described above may also be evaluated for their influence on the lifetime of lymphocytes. Numerous assays for such activity are familiar to those skilled in the art, including the assays disclosed in the following references: Darzynkiewicz et al., Cytometry 13:795-808, 1992; Gorczyca et al., Leukemia 7:659-670, 1993; Gorczyca et al., Cancer Res. 53:1945-1951, 1993; Itoh et al., Cell 66:233-243, 1991; Zacharchuk, J. Immunol. 145:4037-4045, 1990; Zamai et al., Cytometry 14:891-897, 1993; Gorczyca et al., Int. J. Oncol. 1:639-648, 1992.

The proteins or polypeptides prepared as described above may also be evaluated for their influence on early steps of T-cell commitment and development. Numerous assays for such activity are familiar to those skilled in the art, including without limitation the assays disclosed in the following references: Antica et al., Blood 84:111-117, 1994; Fine et al., Cell. Immunol. 155:111-122, 1994; Galy et al., Blood 85:2770-2778, 1995; Toki et al., Proc. Nat. Acad Sci. USA 88:7548-7551, 1991.

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Those proteins or polypeptides which exhibit activity as immune system regulators activity may then be formulated as pharmaceuticals and used to treat clinical conditions in which regulation of immune activity is beneficial. For example, the protein or polypeptide may be useful in the treatment of various immune deficiencies and disorders (including severe combined immunodeficiency), e.g., in regulating (up or down) growth and proliferation of T and/or B lymphocytes, as well as effecting the cytolytic activity of NK cells and other cell populations. These immune deficiencies may be genetic or be caused by viral (e.g., HIV) as well as bacterial or fungal infections, or may result from autoimmune disorders. More specifically, infectious diseases caused by viral, bacterial, fungal or other infection may be treatable using the protein or polypeptide including infections by HIV, hepatitis viruses, herpesviruses, mycobacteria, Leishmania spp., plamodium. and various fungal infections such as candidiasis. Of course, in this regard, a protein or polypeptide may also be useful where a boost to the immune system generally may be desirable, i.e., in the treatment of cancer.

Alternatively, the proteins or polypeptides prepared as described above may be used in treatment of autoimmune disorders including, for example, connective tissue disease, multiple sclerosis, systemic lupus erythematosus, rheumatoid arthritis, autoimmune pulmonary inflammation, Guillain35 Barre syndrome, autoimmune thyroiditis, insulin dependent diabetes mellitis, myasthenia gravis, graft-versus-host disease and autoimmune inflammatory eye disease. Such a protein or polypeptide may also to be useful in the treatment of allergic reactions and conditions, such as asthma (particularly allergic

asthma) or other respiratory problems. Other conditions, in which immune suppression is desired (including, for example, organ transplantation), may also be treatable using the protein or polypeptide.

Using the proteins or polypeptides of the invention it may also be possible to regulate immune responses either up or down. Down regulation may involve inhibiting or blocking an immune response already in progress or may involve preventing the induction of an immune response. The functions of activated T-cells may be inhibited by suppressing T cell responses or by inducing specific tolerance in T cells, or both. Immunosuppression of T cell responses is generally an active non-antigen-specific process which requires continuous exposure of the T cells to the suppressive agent. Tolerance, which involves inducing non-responsiveness or anergy in T cells, is distinguishable from immunosuppression in that it is generally antigen-specific and persists after the end of exposure to the tolerizing agent. Operationally, tolerance can be demonstrated by the lack of a T cell response upon reexposure to specific antigen in the absence of the tolerizing agent.

Down regulating or preventing one or more antigen functions (including without limitation B lymphocyte antigen functions, such as, for example, B7 costimulation), e.g., preventing high level 15 lymphokine synthesis by activated T cells, will be useful in situations of tissue, skin and organ transplantation and in graft-versus-host disease (GVHD). For example, blockage of T cell function should result in reduced tissue destruction in tissue transplantation. Typically, in tissue transplants, rejection of the transplant is initiated through its recognition as foreign by T cells, followed by an immune reaction that destroys the transplant. The administration of a molecule which inhibits or blocks 20 interaction of a B7 lymphocyte antigen with its natural ligand(s) on immune cells (such as a soluble, monomeric form of a peptide having B7-2 activity alone or in conjunction with a monomeric form of a peptide having an activity of another B lymphocyte antigen (e.g., B7-1, B7-3) or blocking antibody), prior to transplantation, can lead to the binding of the molecule to the natural ligand(s) on the immune cells without transmitting the corresponding costimulatory signal. Blocking B lymphocyte antigen 25 function in this matter prevents cytokine synthesis by immune cells, such as T cells, and thus acts as an immunosuppressant. Moreover, the lack of costimulation may also be sufficient to anergize the T cells, thereby inducing tolerance in a subject. Induction of long-term tolerance by B lymphocyte antigenblocking reagents may avoid the necessity of repeated administration of these blocking reagents. To achieve sufficient immunosuppression or tolerance in a subject, it may also be necessary to block the 30 function of a combination of B lymphocyte antigens.

The efficacy of particular blocking reagents in preventing organ transplant rejection or GVHD can be assessed using animal models that are predictive of efficacy in humans. Examples of appropriate systems which can be used include allogeneic cardiac grafts in rats and xenogeneic pancreatic islet cell grafts in mice, both of which have been used to examine the immunosuppressive effects of CTLA4Ig fusion proteins in vivo as described in Lenschow et al., Science 257:789-792 (1992) and Turka et al., Proc. Natl. Acad. Sci USA, 89:11102-11105 (1992). In addition, murine models of GVHD (see Paul ed.,

Fundamental Immunology, Raven Press, New York, 1989, pp. 846-847) can be used to determine the effect of blocking B lymphocyte antigen function in vivo on the development of that disease.

Blocking antigen function may also be therapeutically useful for treating autoimmune diseases. Many autoimmune disorders are the result of inappropriate activation of T cells that are reactive against 5 self tissue and which promote the production of cytokines and autoantibodies involved in the pathology of the diseases. Preventing the activation of autoreactive T cells may reduce or eliminate disease symptoms. Administration of reagents which block costimulation of T cells by disrupting receptor/ligand interactions of B lymphocyte antigens can be used to inhibit T cell activation and prevent production of autoantibodies or T cell-derived cytokines which potentially involved in the disease 10 process. Additionally, blocking reagents may induce antigen-specific tolerance of autoreactive T cells which could lead to long-term relief from the disease. The efficacy of blocking reagents in preventing or alleviating autoimmune disorders can be determined using a number of well-characterized animal models of human autoimmune diseases. Examples include murine experimental autoimmune encephalitis, systemic lupus erythmatosis in MRL/pr/pr mice or NZB hybrid mice, murine autoimmuno 15 collagen arthritis, diabetes mellitus in OD mice and BB rats, and murine experimental myasthenia gravis (see Paul ed., Fundamental Immunology, Raven Press, New York, 1989, pp. 840-856).

Upregulation of an antigen function (preferably a B lymphocyte antigen function), as a means of up regulating immune responses, may also be useful in therapy. Upregulation of immune responses may involve either enhancing an existing immune response or eliciting an initial immune response as shown 20 by the following examples. For instance, enhancing an immune response through stimulating B lymphocyte antigen function may be useful in cases of viral infection. In addition, systemic viral diseases such as influenza, the common cold, and encephalitis might be alleviated by the administration of stimulatory form of B lymphocyte antigens systemically.

Alternatively, antiviral immune responses may be enhanced in an infected patient by removing 25 T cells from the patient, costimulating the T cells in vitro with viral antigen-pulsed APCs either expressing the proteins or polypeptides described above or together with a stimulatory form of the protein or polypeptide and reintroducing the in vitro primed T cells into the patient. The infected cells would now be capable of delivering a costimulatory signal to T cells in vivo, thereby activating the T cells.

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In another application, upregulation or enhancement of antigen function (preferably B lymphocyte antigen function) may be useful in the induction of tumor immunity. Tumor cells (e.g., sarcoma, melanoma, lymphoma, leukemia, neuroblastoma, carcinoma) transfected with one of the above-described nucleic acids encoding a protein or polypeptide can be administered to a subject to overcome tumor-specific tolerance in the subject. If desired, the tumor cell can be transfected to express 35 a combination of peptides. For example, tumor cells obtained from a patient can be transfected ex vivo with an expression vector directing the expression of a peptide having B7-2-like activity alone, or in conjunction with a peptide having B7-1-like activity and/or B7-3-like activity. The transfected tumor

cells are returned to the patient to result in expression of the peptides on the surface of the transfected cell. Alternatively, gene therapy techniques can be used to target a tumor cell for transfection in vivo.

The presence of the protein or polypeptide encoded by the nucleic acids described above having the activity of a B lymphocyte antigen(s) on the surface of the tumor cell provides the necessary 5 costimulation signal to T cells to induce a T cell mediated immune response against the transfected tumor cells. In addition, tumor cells which lack or which fail to reexpress sufficient amounts of MHC class I or MHC class II molecules can be transfected with nucleic acids encoding all or a portion of (e.g., a cytoplasmic-domain truncated portion) of an MHC class I α chain and β₂ microglobulin or an MHC class II α chain and an MHC class II β chain to thereby express MHC class I or MHC class II proteins 10 on the cell surface, respectively. Expression of the appropriate MHC class I or class II molecules in conjunction with a peptide having the activity of a B lymphocyte antigen (e.g., B7-1, B7-2, B7-3) induces a T cell mediated immune response against the transfected tumor cell. Optionally, a nucleic acid encoding an antisense construct which blocks expression of an MHC class II associated protein, such as the invariant chain, can also be cotransfected with a DNA encoding a protein or polypeptide having the 15 activity of a B lymphocyte antigen to promote presentation of tumor associated antigens and induce tumor specific immunity. Thus, the induction of a T cell mediated immune response in a human subject may be sufficient to overcome tumor-specific tolerance in the subject. Alternatively, as described in more detail below, nucleic acids encoding these immune system regulator proteins or polypeptides or nucleic acids regulating the expression of such proteins or polypeptides may be introduced into 20 appropriate host cells to increase or decrease the expression of the proteins as desired.

EXAMPLE 26

Assaying the Expressed Proteins or Polypeptides for Hematopoiesis Regulating Activity

25 The proteins or polypeptides encoded by the nucleic acids described above may also be evaluated for their hematopoiesis regulating activity. For example, the effect of the proteins or polypeptides on embryonic stem cell differentiation may be evaluated. Numerous assays for such activity are familiar to those skilled in the art, including the assays disclosed in the following references: Johansson et al. Cell. Biol. 15:141-151, 1995; Keller et al., Mol. Cell. Biol. 13:473-486, 1993;
30 McClanahan et al., Blood 81:2903-2915, 1993.

The proteins or polypeptides encoded by the nucleic acids described above may also be evaluated for their influence on the lifetime of stem cells and stem cell differentiation. Numerous assays for such activity are familiar to those skilled in the art, including the assays disclosed in the following references: Freshney, M.G. Methylcellulose Colony Forming Assays, in <u>Culture of Hematopoietic Cells</u>.

35 R.I. Freshney, et al. Eds. pp. 265-268, Wiley-Liss, Inc., New York, NY. 1994; Hirayama et al., Proc. Natl. Acad. Sci. USA 89:5907-5911, 1992; McNiece, I.K. and Briddell, R.A. Primitive Hematopoietic Colony Forming Cells with High Proliferative Potential, in <u>Culture of Hematopoietic Cells</u>. supra;

Neben et al., Experimental Hematology 22:353-359, 1994; Ploemacher, R.E. Cobblestone Area Forming Cell Assay, In <u>Culture of Hematopoietic Cells.</u> supra; Spooncer, E., Dexter, M. and Allen, T. Long Term Bone Marrow Cultures in the Presence of Stromal Cells, in <u>Culture of Hematopoietic Cells</u> supra; and Sutherland, H.J. Long Term Culture Initiating Cell Assay, in <u>Culture of Hematopoietic Cells</u>. supra.

Those proteins or polypeptides which exhibit hematopoiesis regulatory activity may then be formulated as pharmaceuticals and used to treat clinical conditions in which regulation of hematopoeisis is beneficial. For example, a protein or polypeptide of the present invention may be useful in regulation of hematopoiesis and, consequently, in the treatment of myeloid or lymphoid cell deficiencies. Evenmarginal biological activity in support of colony forming cells or of factor-dependent cell lines indicates 10 involvement in regulating hematopoiesis, e.g. in supporting the growth and proliferation of erythroid progenitor cells alone or in combination with other cytokines, thereby indicating utility, for example, in treating various anemias or for use in conjunction with irradiation/chemotherapy to stimulate the production of erythroid precursors and/or erythroid cells; in supporting the growth and proliferation of myeloid cells such as granulocytes and monocytes/macrophages (i.e., traditional CSF activity) useful, for 15 example, in conjunction with chemotherapy to prevent or treat consequent myelo-suppression; in supporting the growth and proliferation of megakaryocytes and consequently of platelets thereby allowing prevention or treatment of various platelet disorders such as thrombocytopenia, and generally for use in place of or complimentary to platelet transfusions; and/or in supporting the growth and proliferation of hematopoietic stem cells which are capable of maturing to any and all of the above-20 mentioned hematopoietic cells and therefore find therapeutic utility in various stem cell disorders (such as those usually treated with transplantion, including, without limitation, aplastic anemia and paroxysmal nocturnal hemoglobinuria), as well as in repopulating the stem cell compartment post irradiation/chemotherapy, either in-vivo or ex-vivo (i.e., in conjunction with bone marrow transplantation or with peripheral progenitor cell transplantation (homologous or heterologous)) as 25 normal cells or genetically manipulated for gene therapy. Alternatively, as described in more detail below, nucleic acids encoding these proteins or polypeptides or nucleic acids regulating the expression of these proteins or polypeptides may be introduced into appropriate host cells to increase or decrease the expression of the proteins as desired.

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EXAMPLE 27

Assaying the Expressed Proteins or Polypeptides for Regulation of Tissue Growth

The proteins or polypeptides encoded by the nucleic acids described above may also be evaluated for their effect on tissue growth. Numerous assays for such activity are familiar to those skilled in the art, including the assays disclosed in International Patent Publication No. WO95/16035, International Patent Publication No. WO95/05846 and International Patent Publication No. WO91/07491.

Assays for wound healing activity include, without limitation, those described in: Winter, *Epidermal Wound Healing*, pps. 71-112 (Maibach, H1 and Rovee, DT, eds.), Year Book Medical Publishers, Inc., Chicago, as modified by Eaglstein and Mertz, J. Invest. Dermatol 71:382-84 (1978).

Those proteins or polypeptides which are involved in the regulation of tissue growth may then

5 be formulated as pharmaceuticals and used to treat clinical conditions in which regulation of tissue
growth is beneficial. For example, a protein or polypeptide may have utility in compositions used for
bone, cartilage, tendon, ligament and/or nerve tissue growth or regeneration, as well as for wound
healing and tissue repair and replacement, and in the treatment of burns, incisions and ulcers.

A protein or polypeptide encoded by the nucleic acids described above which induces cartilage and/or bone growth in circumstances where bone is not normally formed, has application in the healing of bone fractures and cartilage damage or defects in humans and other animals. Such a preparation employing a protein or polypeptide of the invention may have prophylactic use in closed as well as open fracture reduction and also in the improved fixation of artificial joints. *De novo* bone synthesis induced by an osteogenic agent contributes to the repair of congenital, trauma induced, or oncologic resection induced craniofacial defects, and also is useful in cosmetic plastic surgery.

A protein or polypeptide of this invention may also be used in the treatment of periodontal disease, and in other tooth repair processes. Such agents may provide an environment to attract bone-forming cells, stimulate growth of bone-forming cells or induce differentiation of progenitors of bone-forming cells. A protein of the invention may also be useful in the treatment of osteoporosis or osteoarthritis, such as through stimulation of bone and/or cartilage repair or by blocking inflammation or processes of tissue destruction (collagenase activity, osteoclast activity, etc.) mediated by inflammatory processes.

Another category of tissue regeneration activity that may be attributable to the proteins or polypeptides encoded by the nucleic acids described above is tendon/ligament formation. A protein or polypeptide encoded by the nucleic acids described above, which induces tendon/ligament-like tissue or other tissue formation in circumstances where such tissue is not normally formed, has application in the healing of tendon or ligament tears, deformities and other tendon or ligament defects in humans and other animals. Such a preparation employing a tendon/ligament-like tissue inducing protein may have prophylactic use in preventing damage to tendon or ligament tissue, as well as use in the improved fixation of tendon or ligament to bone or other tissues, and in repairing defects to tendon or ligament tissue. De novo tendon/ligament-like tissue formation induced by a protein or polypeptide of the present invention contributes to the repair of tendon or ligaments defects of congenital, traumatic or other origin and is also useful in cosmetic plastic surgery for attachment or repair of tendons or ligaments. The proteins or polypeptides of the present invention may provide an environment to attract tendon- or ligament-forming cells, stimulate growth of tendon- or ligament-forming cells, induce differentiation of progenitors of tendon- or ligament-forming cells, or induce growth of tendon/ligament cells or progenitors ex vivo for return *in vivo* to effect tissue repair. The proteins or polypeptides of the

invention may also be useful in the treatment of tendinitis, carpal tunnel syndrome and other tendon or ligament defects. The therapeutic compositions may also include an appropriate matrix and/or sequestering agent as a carrier as is well known in the art.

The proteins or polypeptides of the present invention may also be useful for proliferation of
neural cells and for regeneration of nerve and brain tissue, *i.e.*, for the treatment of central and peripheral
nervous system diseases and neuropathies, as well as mechanical and traumatic disorders, which involve
degeneration, death or trauma to neural cells or nerve tissue. More specifically, a protein or polypeptide
may be used in the treatment of diseases of the peripheral nervous system, such as peripheral nerve
injuries, peripheral neuropathy and localized neuropathies, and central nervous system diseases, such as
Alzheimer's, Parkinson's disease, Huntington's disease, amyotrophic lateral sclerosis, and Shy-Drager
syndrome. Further conditions which may be treated in accordance with the present invention include
mechanical and traumatic disorders, such as spinal cord disorders, head trauma and cerebrovascular
diseases such as stroke. Peripheral neuropathies resulting from chemotherapy or other medical therapies
may also be treatable using a protein or polypeptide of the invention.

Proteins or polypeptides of the invention may also be useful to promote better or faster closure of non-healing wounds, including without limitation pressure ulcers, ulcers associated with vascular insufficiency, surgical and traumatic wounds, and the like.

It is expected that a protein or polypeptide of the present invention may also exhibit activity for generation or regeneration of other tissues, such as organs (including, for example, pancreas, liver, intestine, kidney, skin, endothelium) muscle (smooth, skeletal or cardiac) and vascular (including vascular endothelium) tissue, or for promoting the growth of cells comprising such tissues. Part of the desired effects may be by inhibition or modulation of fibrotic scarring to allow normal tissue to generate. A protein or polypeptide of the invention may also exhibit angiogenic activity.

A protein or polypeptide of the present invention may also be useful for gut protection or regeneration and treatment of lung or liver fibrosis, reperfusion injury in various tissues, and conditions resulting from systemic cytokine damage.

A protein or polypeptide of the present invention may also be useful for promoting or inhibiting differentiation of tissues described above from precursor tissues or cells; or for inhibiting the growth of tissues described above.

Alternatively, as described in more detail below, nucleic acids encoding tissue growth regulating activity proteins or polypeptides or nucleic acids regulating the expression of such proteins or polypeptides may be introduced into appropriate host cells to increase or decrease the expression of the proteins as desired.

EXAMPLE 28

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The proteins or polypeptides of the present invention may also be evaluated for their ability to regulate reproductive hormones, such as follicle stimulating hormone. Numerous assays for such activity are familiar to those skilled in the art, including the assays disclosed in the following references: Vale et al., Endocrinol. 91:562-572, 1972; Ling et al., Nature 321:779-782, 1986; Vale et al., Nature 5 321:776-779, 1986; Mason et al., Nature 318:659-663, 1985; Forage et al., Proc. Natl. Acad. Sci. USA 83:3091-3095, 1986. Chapter 6.12 in Current Protocols in Immunology, J.E. Coligan et al. Eds. Greene Publishing Associates and Wiley-Intersciece; Taub et al. J. Clin. Invest. 95:1370-1376, 1995; Lind et al. APMIS 103:140-146, 1995; Muller et al. Eur. J. Immunol. 25:1744-1748; Gruber et al. J. Immunol. 152:5860-5867, 1994; Johnston et al., J Immunol. 153:1762-1768, 1994.

Those proteins or polypeptides which exhibit activity as reproductive hormones or regulators of cell movement may then be formulated as pharmaceuticals and used to treat clinical conditions in which regulation of reproductive hormones are beneficial. For example, a protein or polypeptide may exhibit activin- or inhibin-related activities. Inhibins are characterized by their ability to inhibit the release of follicle stimulating hormone (FSH), while activins are characterized by their ability to stimulate the 15 release of FSH. Thus, a protein or polypeptide of the present invention, alone or in heterodimers with a member of the inhibin family, may be useful as a contraceptive based on the ability of inhibins to decrease fertility in female mammals and decrease spermatogenesis in male mammals. Administration of sufficient amounts of other inhibins can induce infertility in these mammals. Alternatively, the protein or polypeptide of the invention, as a homodimer or as a heterodimer with other protein subunits 20 of the inhibin-B group, may be useful as a fertility inducing therapeutic, based upon the ability of activin molecules in stimulating FSH release from cells of the anterior pituitary. See, for example, United States Patent 4,798,885. A protein or polypeptide of the invention may also be useful for advancement of the onset of fertility in sexually immature mammals, so as to increase the lifetime reproductive performance of domestic animals such as cows, sheep and pigs.

Alternatively, as described in more detail below, nucleic acids encoding reproductive hormone regulating activity proteins or polypeptides or nucleic acids regulating the expression of such proteins or polypeptides may be introduced into appropriate host cells to increase or decrease the expression of the proteins or polypeptides as desired.

EXAMPLE 29 30

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Assaying the Expressed Proteins or Polypeptides For Chemotactic/Chemokinetic Activity The proteins or polypeptides of the present invention may also be evaluated for chemotactic/chemokinetic activity. For example, a protein or polypeptide of the present invention may have chemotactic or chemokinetic activity (e.g., act as a chemokine) for mammalian cells, including, for 35 example, monocytes, fibroblasts, neutrophils, T-cells, mast cells, eosinophils, epithelial and/or endothelial cells. Chemotactic and chemokinetic proteins or polypeptides can be used to mobilize or attract a desired cell population to a desired site of action. Chemotactic or chemokinetic proteins or

polypeptides provide particular advantages in treatment of wounds and other trauma to tissues, as well as in treatment of localized infections. For example, attraction of lymphocytes, monocytes or neutrophils to tumors or sites of infection may result in improved immune responses against the tumor or infecting agent.

A protein or polypeptide has chemotactic activity for a particular cell population if it can stimulate, directly or indirectly, the directed orientation or movement of such cell population.

Preferably, the protein or polypeptide has the ability to directly stimulate directed movement of cells. Whether a particular protein or polypeptide has chemotactic activity for a population of cells can be readily determined by employing such protein or polypeptide in any known assay for cell chemotaxis.

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The activity of a protein or polypeptide of the invention may, among other means, be measured by the following methods:

Assays for chemotactic activity (which will identify proteins or polypeptides that induce or prevent chemotaxis) consist of assays that measure the ability of a protein or polypeptide to induce the migration of cells across a membrane as well as the ability of a protein or polypeptide to induce the adhesion of one cell population to another cell population. Suitable assays for movement and adhesion include, without limitation, those described in: *Current Protocols in Immunology*, Ed by J.E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W. Strober, Pub. Greene Publishing Associates and Wiley-Interscience, Chapter 6.12: 6.12.1-6.12.28; Taub et al. J. Clin. Invest. 95:1370-1376, 1995; Lind et al. APMIS 103:140-146, 1995; Mueller et al., Eur. J. Immunol. 25:1744-1748; Gruber et al. J. Immunol. 152:5860-5867, 1994; Johnston et al. J. Immunol., 153:1762-1768, 1994.

EXAMPLE 30

Assaying the Expressed Proteins or Polypeptides for Regulation of Blood Clotting

The proteins or polypeptides of the present invention may also be evaluated for their effects on blood clotting. Numerous assays for such activity are familiar to those skilled in the art, including the assays disclosed in the following references: Linet et al., J. Clin. Pharmacol. 26:131-140, 1986; Burdick et al., Thrombosis Res. 45:413-419, 1987; Humphrey et al., Fibrinolysis 5:71-79 (1991); Schaub, Prostaglandins 35:467-474, 1988.

Those proteins or polypeptides which are involved in the regulation of blood clotting may then

30 be formulated as pharmaceuticals and used to treat clinical conditions in which regulation of blood
clotting is beneficial. For example, a protein or polypeptide of the invention may also exhibit hemostatic
or thrombolytic activity. As a result, such a protein or polypeptide is expected to be useful in treatment
of various coagulations disorders (including hereditary disorders, such as hemophilias) or to enhance
coagulation and other hemostatic events in treating wounds resulting from trauma, surgery or other

35 causes. A protein or polypeptide of the invention may also be useful for dissolving or inhibiting
formation of thromboses and for treatment and prevention of conditions resulting therefrom (such as
infarction of cardiac and central nervous system vessels (e.g., stroke)). Alternatively, as described in

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more detail below, nucleic acids encoding blood clotting activity proteins or polypeptides or nucleic acids regulating the expression of such proteins or polypeptides may be introduced into appropriate host cells to increase or decrease the expression of the proteins or polypeptides as desired.

EXAMPLE 31

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Assaying the Expressed Proteins or Polypeptides for Involvement in Receptor/Ligand Interactions

The proteins or polypeptides of the present invention may also be evaluated for their involvement in receptor/ligand interactions. Numerous assays for such involvement are familiar to those 10 skilled in the art, including the assays disclosed in the following references: Chapter 7, 7,28,1-7,28,22) in Current Protocols in Immunology, J.E. Coligan et al. Eds. Greene Publishing Associates and Wiley-Interscience: Takai et al., Proc. Natl. Acad. Sci. USA 84:6864-6868, 1987; Bierer et al., J. Exp. Med. 168:1145-1156, 1988; Rosenstein et al., J. Exp. Med. 169:149-160, 1989; Stoltenborg et al., J. Immunol. Methods 175:59-68, 1994; Stitt et al., Cell 80:661-670, 1995; Gyuris et al., Cell 75:791-803, 1993.

For example, the proteins or polypeptides of the present invention may also demonstrate activity as receptors, receptor ligands or inhibitors or agonists of receptor/ligand interactions. Examples of such receptors and ligands include, without limitation, cytokine receptors and their ligands, receptor kinases and their ligands, receptor phosphatases and their ligands, receptors involved in cell-cell interactions and their ligands (including without limitation, cellular adhesion molecules (such as selectins, integrins and 20 their ligands) and receptor/ligand pairs involved in antigen presentation, antigen recognition and development of cellular and humoral immune responses). Receptors and ligands are also useful for screening of potential peptide or small molecule inhibitors of the relevant receptor/ligand interaction. A protein or polypeptide of the present invention (including, without limitation, fragments of receptors and ligands) may be useful as inhibitors of receptor/ligand interactions. Alternatively, as described in more 25 detail below, nucleic acids encoding proteins or polypeptides involved in receptor/ligand interactions or nucleic acids regulating the expression of such proteins or polypeptides may be introduced into appropriate host cells to increase or decrease the expression of the proteins or polypeptides as desired.

EXAMPLE 32

Assaying the Proteins or Polypeptides for Anti-Inflammatory Activity

The proteins or polypeptides of the present invention may also be evaluated for antiinflammatory activity. The anti-inflammatory activity may be achieved by providing a stimulus to cells involved in the inflammatory response, by inhibiting or promoting cell-cell interactions (such as, for example, cell adhesion), by inhibiting or promoting chemotaxis of cells involved in the 35 inflammatory process, inhibiting or promoting cell extravasation, or by stimulating or suppressing production of other factors which more directly inhibit or promote an inflammatory response. Proteins or polypeptides exhibiting such activities can be used to treat inflammatory conditions

including chronic or acute conditions, including without limitation inflammation associated with infection (such as septic shock, sepsis or systemic inflammatory response syndrome), ischemia-reperfusioninury, endotoxin lethality, arthritis, complement-mediated hyperacute rejection, nephritis, cytokine- or chemokine-induced lung injury, inflammatory bowel disease, Crohn's disease or resulting from over production of cytokines such as TNF or IL-1. Proteins or polypeptides of the invention may also be useful to treat anaphylaxis and hypersensitivity to an antigenic substance or material. Alternatively, as described in more detail below, nucleic acids encoding anti-inflammatory activity proteins or polypeptides or nucleic acids regulating the expression of such proteins or polypeptides may be introduced into appropriate host cells to increase or decrease the expression of the proteins or polypeptides as desired.

EXAMPLE 33

Assaying the Expressed Proteins or Polypeptides for Tumor Inhibition Activity

The proteins or polypeptides of the present invention may also be evaluated for tumor inhibition activity. In addition to the activities described above for immunological treatment or prevention of tumors, a protein or polypeptide of the invention may exhibit other anti-tumor activities. A protein or polypeptide may inhibit tumor growth directly or indirectly (such as, for example, via ADCC). A protein or polypeptide may exhibit its tumor inhibitory activity by acting on tumor tissue or tumor precursor tissue, by inhibiting formation of tissues necessary to support tumor growth (such as, for example, by inhibiting angiogenesis), by causing production of other factors, agents or cell types which inhibit tumor growth, or by suppressing, eliminating or inhibiting factors, agents or cell types which promote tumor growth. Alternatively, as described in more detail below, nucleic acids encoding proteins or polypeptides with tumor inhibition activity or nucleic acids regulating the expression of such proteins or polypeptides may be introduced into appropriate host cells to increase or decrease the expression of the proteins or polypeptides as desired.

A protein or polypeptide of the invention may also exhibit one or more of the following additional activities or effects: inhibiting the growth, infection or function of, or killing, infectious agents, including, without limitation, bacteria, viruses, fungi and other parasites; effecting (suppressing or enhancing) bodily characteristics, including, without limitation, height, weight, hair color, eye color, skin, fat to lean ratio or other tissue pigmentation, or organ or body part size or shape (such as, for example, breast augmentation or diminution, change in bone form or shape); effecting biorhythms or circadian cycles or rhythms; effecting the fertility of male or female subjects; effecting the metabolism, catabolism, anabolism, processing, utilization, storage or climination of dietary fat, lipid, protein, carbohydrate, vitamins, minerals, cofactors or other nutritional factors or component(s); effecting behavioral characteristics, including, without limitation, appetite, libido, stress, cognition (including cognitive disorders), depression (including depressive disorders) and violent behaviors; providing analgesic effects or other pain reducing effects; promoting differentiation and growth of embryonic stem

cells in lineages other than hematopoietic lineages; hormonal or endocrine activity; in the case of enzymes, correcting deficiencies of the enzyme and treating deficiency-related diseases; treatment of hyperproliferative disorders (such as, for example, psoriasis); immunoglobulin-like activity (such as, for example, the ability to bind antigens or complement); and the ability to act as an antigen in a vaccine composition to raise an immune response against such protein or another material or entity which is cross-reactive with such protein. Alternatively, as described in more detail below, nucleic acids encoding proteins or polypeptides involved in any of the above mentioned activities or nucleic acids regulating the expression of such proteins may be introduced into appropriate host cells to increase or decrease the expression of the proteins or polypeptides as desired.

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EXAMPLE 34

<u>Identification of Proteins or Polypeptides which Interact with</u> Proteins or Polypeptides of the Present Invention

Proteins or polypeptides which interact with the proteins or polypeptides of the present

invention, such as receptor proteins, may be identified using two hybrid systems such as the Matchmaker

Two Hybrid System 2 (Catalog No. K1604-1, Clontech). As described in the manual accompanying the

kit, nucleic acids encoding the proteins or polypeptides of the present invention, are inserted into an

expression vector such that they are in frame with DNA encoding the DNA binding domain of the yeast

transcriptional activator GAL4. cDNAs in a cDNA library which encode proteins or polypeptides which

might interact with the proteins or polypeptides of the present invention are inserted into a second

expression vector such that they are in frame with DNA encoding the activation domain of GAL4. The

two expression plasmids are transformed into yeast and the yeast are plated on selection medium which

selects for expression of selectable markers on each of the expression vectors as well as GAL4

dependent expression of the HIS3 gene. Transformants capable of growing on medium lacking histidine

are screened for GAL4 dependent lacZ expression. Those cells which are positive in both the histidine

selection and the lacZ assay contain plasmids encoding proteins or polypeptides which interact with the

proteins or polypeptides of the present invention.

Alternatively, the system described in Lustig et al., Methods in Enzymology 283: 83-99 (1997) may be used for identifying molecules which interact with the proteins or polypeptides of the present invention. In such systems, in vitro transcription reactions are performed on a pool of vectors containing nucleic acid inserts which encode the proteins or polypeptides of the present invention. The nucleic acid inserts are cloned downstream of a promoter which drives in vitro transcription. The resulting pools of mRNAs are introduced into Xenopus laevis oocytes. The oocytes are then assayed for a desired activity.

Alternatively, the pooled *in vitro* transcription products produced as described above may be translated *in vitro*. The pooled *in vitro* translation products can be assayed for a desired activity or for interaction with a known protein or polypeptide.

Proteins, polypeptides or other molecules interacting with proteins or polypeptides of the present invention can be found by a variety of additional techniques. In one method, affinity columns containing the protein or polypeptide of the present invention can be constructed. In some versions, of this method the affinity column contains chimeric proteins in which the protein or polypeptide of the present invention is fused to glutathione S-transferase. A mixture of cellular proteins or pool of expressed proteins as described above and is applied to the affinity column. Molecules interacting with the protein or polypeptide attached to the column can then be isolated and analyzed on 2-D electrophoresis gel as described in Ramunsen et al. Electrophoresis, 18, 588-598 (1997). Alternatively, the molecules retained on the affinity column can be purified by electrophoresis based methods and sequenced. The same method can be used to isolate antibodies, to screen phage display products, or to screen phage display human antibodies.

Molecules interacting with the proteins or polypeptides of the present invention can also be screened by using an Optical Biosensor as described in Edwards & Leatherbarrow, Analytical Biochemistry, 246, 1-6 (1997). The main advantage of the method is that it allows the determination of the association rate between the protein or polypeptide and other interacting molecules. Thus, it is possible to specifically select interacting molecules with a high or low association rate. Typically a target molecule is linked to the sensor surface (through a carboxymethl dextran matrix) and a sample of test molecules is placed in contact with the target molecules. The binding of a test molecule to the target molecule causes a change in the refractive index and/ or thickness. This change is detected by the Biosensor provided it occurs in the evanescent field (which extends a few hundred nanometers from the sensor surface). In these screening assays, the target molecule can be one of the proteins or polypeptides of the present invention and the test sample can be a collection of proteins, polypeptides or other molecules extracted from tissues or cells, a pool of expressed proteins, combinatorial peptide and/ or chemical libraries, or phage displayed peptides. The tissues or cells from which the test

In other methods, a target protein or polypeptide is immobilized and the test population is a collection of unique proteins or polypeptides of the present invention.

To study the interaction of the proteins or polypeptides of the present invention with drugs, the microdialysis coupled to HPLC method described by Wang et al., Chromatographia, 44, 205-208(1997) or the affinity capillary electrophoresis method described by Busch et al., J. Chromatogr. 777:311-328 (1997)can be used.

The system described in U.S. Patent No. 5,654,150 may also be used to identify molecules which interact with the proteins or polypeptides of the present invention. In this system, pools of nucleic acids encoding the proteins or polypeptides of the present invention are transcribed and translated *in*35 vitro and the reaction products are assayed for interaction with a known polypeptide or antibody.

It will be appreciated by those skilled in the art that the proteins or polypeptides of the present invention may be assayed for numerous activities in addition to those specifically enumerated above.

For example, the expressed proteins or polypeptides may be evaluated for applications involving control and regulation of inflammation, tumor proliferation or metastasis, infection, or other clinical conditions. In addition, the proteins or polypeptides may be useful as nutritional agents or cosmetic agents.

The proteins or polypeptides of the present invention may be used to generate antibodies

5 capable of specifically binding to the proteins or polypeptides of the present invention. The
antibodies may be monoclonal antibodies or polyclonal antibodies. As used herein, "antibody" refers
to a polypeptide or group of polypeptides which are comprised of at least one binding domain, where
a binding domain is formed from the folding of variable domains of an antibody molecule to form
three-dimensional binding spaces with an internal surface shape and charge distribution

10 complementary to the features of an antigenic determinant of an antigen., which allows an
immunological reaction with the antigen. Antibodies include recombinant proteins comprising the
binding domains, as wells as fragments, including Fab, Fab', F(ab)2, and F(ab')2 fragments.

As used herein, an "antigenic determinant" is the portion of an antigen molecule, that determines the specificity of the antigen-antibody reaction. An "epitope" refers to an antigenic determinant of a polypeptide. An epitope can comprise as few as 3 amino acids in a spatial conformation which is unique to the epitope. Generally an epitope consists of at least 6 such amino acids, and more usually at least 8-10 such amino acids. Methods for determining the amino acids which make up an epitope include x-ray crystallography, 2-dimensional nuclear magnetic resonance, and epitope mapping e.g. the Pepscan method described by H. Mario Geysen *et al.* 1984. Proc. Natl. Acad. Sci. U.S.A. 81:3998-4002; PCT Publication No. WO 84/03564; and PCT Publication No. WO 84/03506.

In some embodiments, the antibodies may be capable of specifically binding to a protein or polypeptide encoded by EST-related nucleic acids, fragments of EST-related nucleic acids, positional segments of EST-related nucleic acids or fragments of positional segments of EST-related nucleic acids.

In some embodiments, the antibody may be capable of binding an antigenic determinant or an epitope in a protein or polypeptide encoded by EST-related nucleic acids, fragments of EST-related nucleic acids, positional segments of EST-related nucleic acids or fragments of positional segments of EST-related nucleic acids.

In other embodiments, the antibodies may be capable of specifically binding to an EST-related polypeptide, fragment of an EST-related polypeptide, positional segment of an EST-related polypeptide or fragment of a positional segment of an EST-related polypeptide. In some embodiments, the antibody may be capable of binding an antigenic determinant or an epitope in an EST-related polypeptide, fragment of an EST-related polypeptide, positional segment of an EST-related polypeptide or fragment of a positional segment of an EST-related polypeptide.

In the case of secreted proteins, the antibodies may be capable of binding a full-length protein encoded by a nucleic acid of the present invention, a mature protein (i.e. the protein generated by

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cleavage of the signal peptide) encoded by a nucleic acid of the present invention, or a signal peptide encoded by a nucleic acid of the present invention.

EXAMPLE 35

Production of an Antibody to a Human Polypeptide or Protein

The above described EST-related nucleic acids, fragments of EST-related nucleic acids, positional segments of EST-related nucleic acids or fragments of positional segments of EST-related nucleic acids or nucleic acids encoding EST-related polypeptides, fragments of EST-related polypeptides, positional segments of EST-related polypeptides or fragments of positional segments of 10 EST-related polypeptides are operably linked to promoters and introduced into cells as described above.

In the case of secreted proteins, nucleic acids encoding the full protein (i.e. the mature protein and the signal peptide), nucleic acids encoding the mature protein (i.e. the protein generated by cleavage of the signal peptide), or nucleic acids encoding the signal peptide are operably linked to promoters and introduced into cells as described above.

The encoded proteins or polypeptides are then substantially purified or isolated as described 15 · above. The concentration of protein in the final preparation is adjusted, for example, by concentration on an Amicon filter device, to the level of a few µg/ml. Monoclonal or polyclonal antibody to the protein or polypeptide can then be prepared as follows:

1. Monoclonal Antibody Production by Hybridoma Fusion

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Monoclonal antibody to epitopes of any of the proteins or polypeptides identified and isolated as described can be prepared from murine hybridomas according to the classical method of Kohler, and Milstein, Nature 256:495 (1975) or derivative methods thereof. Briefly, a mouse is repetitively inoculated with a few micrograms of the selected protein or peptides derived therefrom over a period of a few weeks. The mouse is then sacrificed, and the antibody producing cells of the spleen isolated. The 25 spleen cells are fused by means of polyethylene glycol with mouse myeloma cells, and the excess unfused cells destroyed by growth of the system on selective media comprising aminopterin (HAT media). The successfully fused cells are diluted and aliquots of the dilution placed in wells of a microtiter plate where growth of the culture is continued. Antibody-producing clones are identified by detection of antibody in the supernatant fluid of the wells by immunoassay procedures, such as Elisa, as 30 originally described by Engvall, Meth. Enzymol. 70:419 (1980). Selected positive clones can be expanded and their monoclonal antibody product harvested for use. Detailed procedures for monoclonal antibody production are described in Davis, L. et al. in Basic Methods in Molecular Biology Elsevier, New York. Section 21-2.

2. Polyclonal Antibody Production by Immunization

Polyclonal antiserum containing antibodies to heterogenous epitopes of a single protein or 35 polypeptide can be prepared by immunizing suitable animals with the expressed protein or peptides derived therefrom, which can be unmodified or modified to enhance immunogenicity. Effective

polyclonal antibody production is affected by many factors related both to the antigen and the host species. For example, small molecules tend to be less immunogenic than others and may require the use of carriers and adjuvant. Also, host animals response vary depending on site of inoculations and doses, with both inadequate or excessive doses of antigen resulting in low titer antisera. Small doses (ng level) of antigen administered at multiple intradermal sites appears to be most reliable. An effective immunization protocol for rabbits can be found in Vaitukaitis. et al.J. Clin. Endocrinol. Metab. 33:988-991 (1971).

Booster injections can be given at regular intervals, and antiserum harvested when antibody titer thereof, as determined semi-quantitatively, for example, by double immunodiffusion in agar against look known concentrations of the antigen, begins to fall. See, for example, Ouchterlony, et al., Chap. 19 in: Handbook of Experimental Immunology D. Wier (ed) Blackwell (1973). Plateau concentration of antibody is usually in the range of 0.1 to 0.2 mg/ml of serum (about 12 µM). Affinity of the antisera for the antigen is determined by preparing competitive binding curves, as described, for example, by Fisher, D., Chap. 42 in: Manual of Clinical Immunology, 2d Ed. (Rose and Friedman, Eds.) Amer. Soc. For Microbiol., Washington, D.C. (1980).

Antibody preparations prepared according to either of the above protocols are useful in a variety of contexts. In particular, the antibodies may be used in immunoaffinity chromatography techniques such as those described below to facilitate large scale isolation, purification, or enrichment of the proteins or polypeptides encoded by EST-related nucleic acids, positional segments of EST-related nucleic acids or fragments of positional segments of EST-related nucleic acids or for the isolation, purification or enrichment of EST-related polypeptides, fragments of EST-related polypeptides, positional segments of EST-related polypeptides or fragments of positional segments of EST-related polypeptides.

In the case of secreted proteins, the antibodies may be used for the isolation, purification, or enrichment of the full protein (*i.e.* the mature protein and the signal peptide), the mature protein (*i.e.* the protein generated by cleavage of the signal peptide), or the signal peptide are operably linked to promoters and introduced into cells as described above.

Additionally, the antibodies may be used in immunoaffinity chromatography techniques such as those described below to isolate, purify, or enrich polypeptides which have been linked to the proteins or polypeptides encoded by EST-related nucleic acids, positional segments of EST-related nucleic acids or fragments of positional segments of EST-related nucleic acids or to isolate, purify, or enrich EST-related polypeptides, fragments of EST-related polypeptides, positional segments of EST-related polypeptides or fragments of positional segments of EST-related polypeptides.

The antibodies may also be used to determine the cellular localization of polypeptides encoded by the proteins or polypeptides encoded by EST-related nucleic acids, positional segments of EST-related nucleic acids or fragments of positional segments of EST-related nucleic acids or the cellular

localization of EST-related polypeptides, fragments of EST-related polypeptides, positional segments of EST-related polypeptides or fragments of positional segments of EST-related polypeptides.

In addition, the antibodies may also be used to determine the cellular localization of polypeptides which have been linked to the proteins or polypeptides encoded by EST-related nucleic acids, positional segments of EST-related nucleic acids or fragments of positional segments of EST-related nucleic acids or polypeptides which have been linked to EST-related polypeptides, fragments of EST-related polypeptides, positional segments of EST-related polypeptides or fragments of positional segments of EST-related polypeptides.

The antibodies may also be used in quantitative immunoassays which determine concentrations
of antigen-bearing substances in biological samples; they may also used semi-quantitatively or
qualitatively to identify the presence of antigen in a biological sample or to identify the type of tissue
present in a biological sample. The antibodies may also be used in therapeutic compositions for killing
cells expressing the protein or reducing the levels of the protein in the body.

15 VI. Use of 5'ESTs or Consensus Contigated 5' ESTs or Sequences Obtainable Therefrom or Portions Thereof as Reagents

The EST-related nucleic acids, positional segments of EST-related nucleic acids or fragments of positional segments of EST-related nucleic acids may be used as reagents in isolation procedures, diagnostic assays, and forensic procedures. For example, sequences from the EST-related nucleic acids, positional segments of EST-related nucleic acids or fragments of positional segments of EST-related nucleic acids, may be detectably labeled and used as probes to isolate other sequences capable of hybridizing to them. In addition, the EST-related nucleic acids, positional segments of EST-related nucleic acids or fragments of positional segments of EST-related nucleic acids may be used to design PCR primers to be used in isolation, diagnostic, or forensic procedures.

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1. Use of EST-related nucleic acids, positional segments of EST-related nucleic acids or fragments of positional segments of EST-related nucleic acids in isolation, diagnostic and forensic procedures

EXAMPLE 36

Preparation of PCR Primers and Amplification of DNA

The EST-related nucleic acids, positional segments of EST-related nucleic acids or fragments of positional segments of EST-related nucleic acids may be used to prepare PCR primers for a variety of applications, including isolation procedures for cloning nucleic acids capable of hybridizing to such sequences, diagnostic techniques and forensic techniques. In some embodiments, the PCR primers at least 10, 15, 18, 20, 23, 25, 28, 30, 40, or 50 nucleotides in length. In some embodiments, the PCR primers may be more than 30 bases in length. It is preferred that the primer pairs have approximately the same G/C ratio, so that melting temperatures are approximately the same. A variety of PCR techniques are familiar to those skilled in the art. For a review of PCR technology, see Molecular Cloning to

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Genetic Engineering White, B.A. Ed. in Methods in Molecular Biology 67: Humana Press, Totowa 1997. In each of these PCR procedures, PCR primers on either side of the nucleic acid sequences to be amplified are added to a suitably prepared nucleic acid sample along with dNTPs and a thermostable polymerase such as Taq polymerase, Pfu polymerase, or Vent polymerase. The nucleic acid in the sample is denatured and the PCR primers are specifically hybridized to complementary nucleic acid sequences in the sample. The hybridized primers are extended. Thereafter, another cycle of denaturation, hybridization, and extension is initiated. The cycles are repeated multiple times to produce an amplified fragment containing the nucleic acid sequence between the primer sites.

10 EXAMPLE 37

Use of the EST-related nucleic acids, positional segments of EST-related nucleic acids or fragments of positional segments of EST-related nucleic acids as probes

Probes derived from EST-related nucleic acids, positional segments of EST-related nucleic acids or fragments of positional segments of EST-related nucleic acids may be labeled with detectable labels

15 familiar to those skilled in the art, including radioisotopes and non-radioactive labels, to provide a detectable probe. The detectable probe may be single stranded or double stranded and may be made using techniques known in the art, including *in vitro* transcription, nick translation, or kinase reactions. A nucleic acid sample containing a sequence capable of hybridizing to the labeled probe is contacted with the labeled probe. If the nucleic acid in the sample is double stranded, it may be denatured prior to contacting the probe. In some applications, the nucleic acid sample may be immobilized on a surface such as a nitrocellulose or nylon membrane. The nucleic acid sample may comprise nucleic acids obtained from a variety of sources, including genomic DNA, cDNA libraries, RNA, or tissue samples.

Procedures used to detect the presence of nucleic acids capable of hybridizing to the detectable probe include well known techniques such as Southern blotting, Northern blotting, dot blotting, colony hybridization, and plaque hybridization. In some applications, the nucleic acid capable of hybridizing to the labeled probe may be cloned into vectors such as expression vectors, sequencing vectors, or *in vitro* transcription vectors to facilitate the characterization and expression of the hybridizing nucleic acids in the sample. For example, such techniques may be used to isolate and clone sequences in a genomic library or cDNA library which are capable of hybridizing to the detectable probe as described in Example 20 above.

PCR primers made as described in Example 36 above may be used in forensic analyses, such as the DNA fingerprinting techniques described in Examples 38-42 below. Such analyses may utilize detectable probes or primers based on the sequences of the EST-related nucleic acids, positional segments of EST-related nucleic acids or fragments of positional segments of EST-related nucleic acids.

In one exemplary method, DNA samples are isolated from forensic specimens of, for example, hair, semen, blood or skin cells by conventional methods. A panel of PCR primers based on a number of the EST-related nucleic acids, positional segments of EST-related nucleic acids or fragments of positional segments of EST-related nucleic acids is then utilized in accordance with Example 36 to amplify DNA of approximately 100-200 bases in length from the forensic specimen. Corresponding sequences are obtained from a test subject. Each of these identification DNAs is then sequenced using standard techniques, and a simple database comparison determines the differences, if any, between the sequences from the subject and those from the sample. Statistically significant differences between the suspect's DNA sequences and those from the sample conclusively prove a lack of identity. This lack of identity can be proven, for example, with only one sequence. Identity, on the other hand, should be demonstrated with a large number of sequences, all matching. Preferably, a minimum of 50 statistically identical sequences of 100 bases in length are used to prove identity between the suspect and the sample.

EXAMPLE 39

Positive Identification by DNA Sequencing

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The technique outlined in the previous example may also be used on a larger scale to provide a unique fingerprint-type identification of any individual. In this technique, primers are prepared from a large number of EST-related nucleic acids, positional segments of EST-related nucleic acids or fragments of positional segments of EST-related nucleic acids. Preferably, 20 to 50 different primers are used. These primers are used to obtain a corresponding number of PCR-generated DNA segments from the individual in question in accordance with Example 34. Each of these DNA segments is sequenced, using the methods set forth in Example 36. The database of sequences generated through this procedure uniquely identifies the individual from whom the sequences were obtained. The same panel of primers may then be used at any later time to absolutely correlate tissue or other biological specimen with that individual.

EXAMPLE 40

Southern Blot Forensic Identification

The procedure of Example 38 is repeated to obtain a panel of at least 10 amplified sequences

from an individual and a specimen. Preferably, the panel contains at least 50 amplified sequences. More
preferably, the panel contains 100 amplified sequences. In some embodiments, the panel contains 200
amplified sequences. This PCR-generated DNA is then digested with one or a combination of,
preferably, four base specific restriction enzymes. Such enzymes are commercially available and known
to those of skill in the art. After digestion, the resultant gene fragments are size separated in multiple

duplicate wells on an agarose gel and transferred to nitrocellulose using Southern blotting techniques
well known to those with skill in the art. For a review of Southern blotting see Davis et al. (Basic
Methods in Molecular Biology, 1986, Elsevier Press. pp 62-65).

A panel of probes based on the sequences of the EST-related nucleic acids, positional segments of EST-related nucleic acids or fragments of positional segments of EST-related nucleic acids are radioactively or colorimetrically labeled using methods known in the art, such as nick translation or end labeling, and hybridized to the Southern blot using techniques known in the art (Davis et al., supra).

5 Preferably, the probe is at least 10, 12, 15, 18, 20, 25, 28, 30, 35, 40, 50, 75, 100, 150, 200, 300, 400 or 500 nucleotides in length. Preferably, the probes are at least 10, 12, 15, 18, 20, 25, 28, 30, 35, 40, 50, 75, 100, 150, 200, 300, 400 or 500 nucleotides in length. In some embodiments, the probes are oligonucleotides which are 40 nucleotides in length or less.

Preferably, at least 5 to 10 of these labeled probes are used, and more preferably at least about 20 or 30 are used to provide a unique pattern. The resultant bands appearing from the hybridization of a large sample of EST-related nucleic acids, positional segments of EST-related nucleic acids or fragments of positional segments of EST-related nucleic acids will be a unique identifier. Since the restriction enzyme cleavage will be different for every individual, the band pattern on the Southern blot will also be unique. Increasing the number of probes will provide a statistically higher level of confidence in the identification since there will be an increased number of sets of bands used for identification.

EXAMPLE 41

Dot Blot Identification Procedure

Another technique for identifying individuals using the EST-related nucleic acids, positional segments of EST-related nucleic acids or fragments of positional segments of EST-related nucleic acids disclosed herein utilizes a dot blot hybridization technique.

Genomic DNA is isolated from nuclei of subject to be identified. Probes are prepared that correspond to at least 10, preferably 50 sequences from the EST-related nucleic acids, positional segments of EST-related nucleic acids or fragments of positional segments of EST-related nucleic acids.

- The probes are used to hybridize to the genomic DNA through conditions known to those in the art. The oligonucleotides are end labeled with P³² using polynucleotide kinase (Pharmacia). Dot Blots are created by spotting the genomic DNA onto nitrocellulose or the like using a vacuum dot blot manifold (BioRad, Richmond California). The nitrocellulose filter containing the genomic sequences is baked or UV linked to the filter, prehybridized and hybridized with labeled probe using techniques known in the art (Davis et
- 30 al., supra). The ³²P labeled DNA fragments are sequentially hybridized with successively stringent conditions to detect minimal differences between the 30 bp sequence and the DNA.
 - Tetramethylammonium chloride is useful for identifying clones containing small numbers of nucleotide mismatches (Wood et al., Proc. Natl. Acad. Sci. USA 82(6):1585-1588 (1985)). A unique pattern of dots distinguishes one individual from another individual.
- EST-related nucleic acids, positional segments of EST-related nucleic acids or fragments of positional segments of EST-related nucleic acids can be used as probes in the following alternative

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fingerprinting technique. In some embodiments, the probes are oligonucleotides which are 40 nucleotides in length or less.

Preferably, a plurality of probes having sequences from different EST-related nucleic acids, positional segments of EST-related nucleic acids or fragments of positional segments of EST-related nucleic acids are used in the alternative fingerprinting technique. Example 42 below provides a representative alternative fingerprinting procedure in which the probes are derived from EST-related nucleic acids, positional segments of EST-related nucleic acids or fragments of positional segments of EST-related nucleic acids.

10 EXAMPLE 42

Alternative "Fingerprint" Identification Technique

Oligonucleotides are prepared from a large number, e.g. 50, 100, or 200, EST-related nucleic acids, positional segments of EST-related nucleic acids or fragments of positional segments of EST-related nucleic acids using commercially available oligonucleotide services such as Genset, Paris,

15 France. Preferably, the oligonucleotides are at least 10, 15, 18, 20, 23, 25 28, or 30 nucleotides in length. However, in some embodiments, the oligonucleotides may be more than 40, 50, 60 or 70 nucleotides in length.

Cell samples from the test subject are processed for DNA using techniques well known to those with skill in the art. The nucleic acid is digested with restriction enzymes such as EcoRI and XbaI.

20 Following digestion, samples are applied to wells for electrophoresis. The procedure, as known in the art, may be modified to accommodate polyacrylamide electrophoresis, however in this example, samples containing 5 ug of DNA are loaded into wells and separated on 0.8% agarose gels. The gels are transferred onto nitrocellulose using standard Southern blotting techniques.

10 ng of each of the oligonucleotides are pooled and end-labeled with P³². The nitrocellulose is prehybridized with blocking solution and hybridized with the labeled probes. Following hybridization and washing, the nitrocellulose filter is exposed to X-Omat AR X-ray film. The resulting hybridization pattern will be unique for each individual.

It is additionally contemplated within this example that the number of probe sequences used can be varied for additional accuracy or clarity.

In addition to their applications in forensics and identification, EST-related nucleic acids, positional segments of EST-related nucleic acids or fragments of positional segments of EST-related nucleic acids may be mapped to their chromosomal locations. Example 41 below describes radiation hybrid (RH) mapping of human chromosomal regions using EST-related nucleic acids, positional segments of EST-related nucleic acids or fragments of positional segments of EST-related nucleic acids.

Example 42 below describes a representative procedure for mapping EST-related nucleic acids, positional segments of EST-related nucleic acids or fragments of positional segments of EST-related nucleic acids.

nucleic acids to their locations on human chromosomes. Example 43 below describes mapping of

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EST-related nucleic acids, positional segments of EST-related nucleic acids or fragments of positional segments of EST-related nucleic acids on metaphase chromosomes by Fluorescence In Situ Hybridization (FISH).

2. Use of EST-related nucleic acids, positional segments of EST-related nucleic acids or fragments of positional segments of EST-related nucleic acids in Chromosome Mapping

EXAMPLE 43

Radiation hybrid mapping of EST-related nucleic acids, positional segments of EST-related nucleic acids or fragments of positional segments of

10 <u>EST-related nucleic acids to the human genome</u>

Radiation hybrid (RH) mapping is a somatic cell genetic approach that can be used for high resolution mapping of the human genome. In this approach, cell lines containing one or more human chromosomes are lethally irradiated, breaking each chromosome into fragments whose size depends on the radiation dose. These fragments are rescued by fusion with cultured rodent cells, yielding subclones containing different portions of the human genome. This technique is described by Benham et al. (Genomics 4:509-517, 1989) and Cox et al., (Science 250:245-250, 1990). The random and independent nature of the subclones permits efficient mapping of any human genome marker. Human DNA isolated from a panel of 80-100 cell lines provides a mapping reagent for ordering EST-related nucleic acids, positional segments of EST-related nucleic acids or fragments of positional segments of EST-related nucleic acids. In this approach, the frequency of breakage between markers is used to measure distance, allowing construction of fine resolution maps as has been done using conventional ESTs (Schuler et al., Science 274:540-546, 1996).

RH mapping has been used to generate a high-resolution whole genome radiation hybrid map of human chromosome 17q22-q25.3 across the genes for growth hormone (GH) and thymidine kinase (TK) (Foster et al., Genomics 33:185-192, 1996), the region surrounding the Gorlin syndrome gene (Obermayr et al., Eur. J. Hum. Genet. 4:242-245, 1996), 60 loci covering the entire short arm of chromosome 12 (Raeymaekers et al., Genomics 29:170-178, 1995), the region of human chromosome 22 containing the neurofibromatosis type 2 locus (Frazer et al., Genomics 14:574-584, 1992) and 13 loci on the long arm of chromosome 5 (Warrington et al., Genomics 11:701-708, 1991).

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EXAMPLE 44

Mapping of EST-related nucleic acids, positional segments of

EST-related nucleic acids or fragments of positional segments of

EST-related nucleic acids to Human Chromosomes using PCR techniques

EST-related nucleic acids, positional segments of EST-related nucleic acids or fragments of positional segments of EST-related nucleic acids may be assigned to human chromosomes using PCR based methodologies. In such approaches, oligonucleotide primer pairs are designed from EST-related

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nucleic acids, positional segments of EST-related nucleic acids or fragments of positional segments of EST-related nucleic acids to minimize the chance of amplifying through an intron. Preferably, the oligonucleotide primers are 18-23 bp in length and are designed for PCR amplification. The creation of PCR primers from known sequences is well known to those with skill in the art. For a review of PCR technology see Erlich. in PCR Technology; Principles and Applications for DNA Amplification. 1992. W.H. Freeman and Co., New York.

The primers are used in polymerase chain reactions (PCR) to amplify templates from total human genomic DNA. PCR conditions are as follows: 60 ng of genomic DNA is used as a template for PCR with 80 ng of each oligonucleotide primer, 0.6 unit of Taq polymerase, and 1 μCu of a 32P-labeled deoxycytidine triphosphate. The PCR is performed in a microplate thermocycler (Techne) under the following conditions: 30 cycles of 94°C, 1.4 min; 55°C, 2 min; and 72°C, 2 min; with a final extension at 72°C for 10 min. The amplified products are analyzed on a 6% polyacrylamide sequencing gel and visualized by autoradiography. If the length of the resulting PCR product is identical to the distance between the ends of the primer sequences in the 5'EST from which the primers are derived, then the PCR reaction is repeated with DNA templates from two panels of human-rodent somatic cell hybrids, BIOS PCRable DNA (BIOS Corporation) and NIGMS Human-Rodent Somatic Cell Hybrid Mapping Panel Number 1 (NIGMS, Camden, NJ).

PCR is used to screen a series of somatic cell hybrid cell lines containing defined sets of human chromosomes for the presence of a given 5'EST. DNA is isolated from the somatic hybrids and used as starting templates for PCR_reactions using the primer pairs from the EST-related nucleic acids, positional segments of EST-related nucleic acids or fragments of positional segments of EST-related nucleic acids. Only those somatic cell hybrids with chromosomes containing the human gene corresponding to the EST-related nucleic acids, positional segments of EST-related nucleic acids or fragments of positional segments of EST-related nucleic acids will yield an amplified fragment. The 5'ESTs are assigned to a chromosome by analysis of the segregation pattern of PCR products from the somatic hybrid DNA templates. The single human chromosome present in all cell hybrids that give rise to an amplified fragment is the chromosome containing that EST-related nucleic acids, positional segments of EST-related nucleic acids or fragments of positional segments of EST-related nucleic acids. For a review of techniques and analysis of results from somatic cell gene mapping experiments. (See Ledbetter *et al.*, Genomics 6:475-481 (1990)).

Alternatively, the EST-related nucleic acids, positional segments of EST-related nucleic acids or fragments of positional segments of EST-related nucleic acids may be mapped to individual chromosomes using FISH as described in Example 45 below.

EXAMPLE 45

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Mapping of EST-related nucleic acids, positional segments of EST-related nucleic acids or fragments of positional segments of

EST-related nucleic acids to Chromosomes Using

Fluorescence In Situ Hybridization

Fluorescence in situ hybridization allows the EST-related nucleic acids, positional segments of EST-related nucleic acids or fragments of positional segments of EST-related nucleic acids to be mapped to a particular location on a given chromosome. The chromosomes to be used for fluorescence in situ hybridization techniques may be obtained from a variety of sources including cell cultures, tissues, or whole blood.

In a preferred embodiment, chromosomal localization of EST-related nucleic acids, positional segments of EST-related nucleic acids or fragments of positional segments of EST-related nucleic acids 10 are obtained by FISH as described by Cherif et al. (Proc. Natl. Acad. Sci. U.S.A., 87:6639-6643, 1990). Metaphase chromosomes are prepared from phytohemagglutinin (PHA)-stimulated blood cell donors. PHA-stimulated lymphocytes from healthy males are cultured for 72 h in RPMI-1640 medium. For synchronization, methotrexate (10 µM) is added for 17 h, followed by addition of 5-bromodeoxyuridine (5-BrdU, 0.1 mM) for 6 h. Colcemid (1 µg/ml) is added for the last 15 min before harvesting the cells. 15 Cells are collected, washed in RPMI, incubated with a hypotonic solution of KCI (75 mM) at 37°C for 15 min and fixed in three changes of methanol:acetic acid (3:1). The cell suspension is dropped onto a glass slide and air dried. The EST-related nucleic acids, positional segments of EST-related nucleic acids or fragments of positional segments of EST-related nucleic acids is labeled with biotin-16 dUTP by nick translation according to the manufacturer's instructions (Bethesda Research Laboratories, Bethesda, 20 MD), purified using a Sephadex G-50 column (Pharmacia, Upsala, Sweden) and precipitated. Just prior to hybridization, the DNA pellet is dissolved in hybridization buffer (50% formamide, 2 X SSC, 10% dextran sulfate, 1 mg/ml sonicated salmon sperm DNA, pH 7) and the probe is denatured at 70°C for 5-10 min.

Slides kept at -20°C are treated for 1 h at 37°C with RNase A (100 µg/ml), rinsed three times in 2 X SSC and dehydrated in an ethanol series. Chromosome preparations are denatured in 70% formamide, 2 X SSC for 2 min at 70°C, then dehydrated at 4°C. The slides are treated with proteinase K (10 µg/100 ml in 20 mM Tris-HCl, 2 mM CaCl₂) at 37°C for 8 min and dehydrated. The hybridization mixture containing the probe is placed on the slide, covered with a coverslip, sealed with rubber cement and incubated overnight in a humid chamber at 37°C. After hybridization and post-hybridization washes, the biotinylated probe is detected by avidin-FITC and amplified with additional layers of biotinylated goat anti-avidin and avidin-FITC. For chromosomal localization, fluorescent R-bands are obtained as previously described (Cherif et al., supra.). The slides are observed under a LEICA fluorescence microscope (DMRXA). Chromosomes are counterstained with propidium iodide and the fluorescent signal of the probe appears as two symmetrical yellow-green spots on both chromatids of the fluorescent R-band chromosome (red). Thus, a particular EST-related nucleic acids, positional segments of EST-related nucleic acids or fragments of positional segments of EST-related nucleic acids may be localized to a particular cytogenetic R-band on a given chromosome.

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Once the EST-related nucleic acids, positional segments of EST-related nucleic acids or fragments of positional segments of EST-related nucleic acids have been assigned to particular chromosomes using the techniques described in Examples 42-44 above, they may be utilized to construct a high resolution map of the chromosomes on which they are located or to identify the chromosomes in a 5 sample.

EXAMPLE 46

Use of EST-related nucleic acids, positional segments of EST-related nucleic acids or fragments of positional segments of EST-related nucleic acids to Construct or Expand Chromosome Maps

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Chromosome mapping involves assigning a given unique sequence to a particular chromosome as described above. Once the unique sequence has been mapped to a given chromosome, it is ordered relative to other unique sequences located on the same chromosome. One approach to chromosome mapping utilizes a series of yeast artificial chromosomes (YACs) bearing several thousand long inserts derived from the chromosomes of the organism from which the EST-related nucleic acids, positional 15 segments of EST-related nucleic acids or fragments of positional segments of EST-related nucleic acids are obtained. This approach is described in Ramaiah Nagaraja et al., Genome Research 7:210-222, March 1997. Briefly, in this approach each chromosome is broken into overlapping pieces which are inserted into the YAC vector. The YAC inserts are screened using PCR or other methods to determine whether they include the EST-related nucleic acids, positional segments of EST-related nucleic acids or 20 fragments of positional segments of EST-related nucleic acids whose position is to be determined. Once an insert has been found which includes the 5'EST, the insert can be analyzed by PCR or other methods to determine whether the insert also contains other sequences known to be on the chromosome or in the region from which the EST-related nucleic acids, positional segments of EST-related nucleic acids or fragments of positional segments of EST-related nucleic acids was derived. This process can be 25 repeated for each insert in the YAC library to determine the location of each of the EST-related nucleic acids, positional segments of EST-related nucleic acids or fragments of positional segments of ESTrelated nucleic acids relative to one another and to other known chromosomal markers. In this way, a high resolution map of the distribution of numerous unique markers along each of the organisms chromosomes may be obtained.

As described in Example 47 below EST-related nucleic acids, positional segments of ESTrelated nucleic acids or fragments of positional segments of EST-related nucleic acids may also be used to identify genes associated with a particular phenotype, such as hereditary disease or drug response.

3. Use of EST-related nucleic acids, positional segments of EST-related nucleic acids or fragments of 35 positional segments of EST-related nucleic acids Gene Identification

EXAMPLE 47

Identification of genes associated with hereditary diseases or drug response

This example illustrates an approach useful for the association of EST-related nucleic acids, positional segments of EST-related nucleic acids or fragments of positional segments of EST-related nucleic acids with particular phenotypic characteristics. In this example, a particular EST-related nucleic acids, positional segments of EST-related nucleic acids or fragments of positional segments of EST-related nucleic acids is used as a test probe to associate that EST-related nucleic acids, positional segments of EST-related nucleic acids or fragments of positional segments of EST-related nucleic acids with a particular phenotypic characteristic.

EST-related nucleic acids, positional segments of EST-related nucleic acids or fragments of positional segments of EST-related nucleic acids are mapped to a particular location on a human chromosome using techniques such as those described in Examples 41 and 42 or other techniques known in the art. A search of Mendelian Inheritance in Man (V. McKusick, Mendelian Inheritance in Man (available on line through Johns Hopkins University Welch Medical Library) reveals the region of the human chromosome which contains the EST-related nucleic acids, positional segments of EST-related nucleic acids or fragments of positional segments of EST-related nucleic acids to be a very gene rich region containing several known genes and several diseases or phenotypes for which genes have not been identified. The gene corresponding to this EST-related nucleic acids, positional segments of EST-related nucleic acids or fragments of positional segments of EST-related nucleic acids thus becomes an immediate candidate for each of these genetic diseases.

Cells from patients with these diseases or phenotypes are isolated and expanded in culture. PCR primers from the EST-related nucleic acids, positional segments of EST-related nucleic acids or fragments of positional segments of EST-related nucleic acids are used to screen genomic DNA, mRNA or cDNA obtained from the patients. EST-related nucleic acids, positional segments of EST-related nucleic acids or fragments of positional segments of EST-related nucleic acids that are not amplified in the patients can be positively associated with a particular disease by further analysis. Alternatively, the PCR analysis may yield fragments of different lengths when the samples are derived from an individual having the phenotype associated with the disease than when the sample is derived from a healthy individual, indicating that the gene containing the EST-related nucleic acids, positional segments of EST-related nucleic acids or fragments of positional segments of EST-related nucleic acids may be responsible for the genetic disease.

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VII. Use of EST-related nucleic acids, positional segments of EST-related nucleic acids or fragments of positional segments of EST-related nucleic acids to Construct Vectors

The present EST-related nucleic acids, positional segments of EST-related nucleic acids or fragments of positional segments of EST-related nucleic acids may also be used to construct secretion vectors capable of directing the secretion of the proteins encoded by genes therein. Such secretion vectors may facilitate the purification or enrichment of the proteins encoded by genes inserted therein by

reducing the number of background proteins from which the desired protein must be purified or enriched. Exemplary secretion vectors are described in Example 48 below.

1. Construction of secretion vectors

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EXAMPLE 48

Construction of Secretion Vectors

The secretion vectors of the present invention include a promoter capable of directing gene expression in the host cell, tissue, or organism of interest. Such promoters include the Rous Sarcoma Virus promoter, the SV40 promoter, the human cytomegalovirus promoter, and other promoters familiar to those skilled in the art.

A signal sequence from one of the EST-related nucleic acids, positional segments of ESTrelated nucleic acids or fragments of positional segments of EST-related nucleic acids is operably linked to the promoter such that the mRNA transcribed from the promoter will direct the translation of the signal peptide. Preferably, the signal sequence is from one of the nucleic acids of SEQ ID NOs.24-811. The host cell, tissue, or organism may be any cell, tissue, or organism which recognizes the signal 15 peptide encoded by the signal sequence in the EST-related nucleic acids, positional segments of ESTrelated nucleic acids or fragments of positional segments of EST-related nucleic acids. Suitable hosts include mammalian cells, tissues or organisms, avian cells, tissues, or organisms, insect cells, tissues or organisms, or yeast.

In addition, the secretion vector contains cloning sites for inserting genes encoding the proteins 20 which are to be secreted. The cloning sites facilitate the cloning of the insert gene in frame with the signal sequence such that a fusion protein in which the signal peptide is fused to the protein encoded by the inserted gene is expressed from the mRNA transcribed from the promoter. The signal peptide directs the extracellular secretion of the fusion protein.

The secretion vector may be DNA or RNA and may integrate into the chromosome of the host, 25 be stably maintained as an extrachromosomal replicon in the host, be an artificial chromosome, or be transiently present in the host. Preferably, the secretion vector is maintained in multiple copies in each host cell. As used herein, multiple copies means at least 2, 5, 10, 20, 25, 50 or more than 50 copies per cell. In some embodiments, the multiple copies are maintained extrachromosomally. In other embodiments, the multiple copies result from amplification of a chromosomal sequence.

Many nucleic acid backbones suitable for use as secretion vectors are known to those skilled in the art, including retroviral vectors, SV40 vectors, Bovine Papilloma Virus vectors, yeast integrating plasmids, yeast episomal plasmids, yeast artificial chromosomes, human artificial chromosomes, P element vectors, baculovirus vectors, or bacterial plasmids capable of being transiently introduced into the host.

The secretion vector may also contain a polyA signal such that the polyA signal is located downstream of the gene inserted into the secretion vector.

After the gene encoding the protein for which secretion is desired is inserted into the secretion vector, the secretion vector is introduced into the host cell, tissue, or organism using calcium phosphate precipitation, DEAE-Dextran, electroporation, liposome-mediated transfection, viral particles or as naked DNA. The protein encoded by the inserted gene is then purified or enriched from the supernatant 5 using conventional techniques such as ammonium sulfate precipitation, immunoprecipitation, immunoaffinitychromatography, size exclusion chromatography, ion exchange chromatography, and HPLC. Alternatively, the secreted protein may be in a sufficiently enriched or pure state in the supernatant or growth media of the host to permit it to be used for its intended purpose without further enrichment.

The signal sequences may also be inserted into vectors designed for gene therapy. In such vectors, the signal sequence is operably linked to a promoter such that mRNA transcribed from the promoter encodes the signal peptide. A cloning site is located downstream of the signal sequence such that a gene encoding a protein whose secretion is desired may readily be inserted into the vector and fused to the signal sequence. The vector is introduced into an appropriate host cell. The protein 15 expressed from the promoter is secreted extracellularly, thereby producing a therapeutic effect.

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EXAMPLE 49

Fusion Vectors

The EST-related nucleic acids, positional segments of EST-related nucleic acids or fragments of 20 positional segments of EST-related nucleic acids may be used to construct fusion vectors for the expression of chimeric polypeptides. The chimeric polypeptides comprise a first polypeptide portion and a second polypeptide portion. In the fusion vectors of the present invention, nucleic acids encoding the first polypeptide portion and the second polypeptide portion are joined in frame with one another so as to generate a nucleic acid encoding the chimeric polypeptide. The nucleic acid encoding the chimeric 25 polypeptide is operably linked to a promoter which directs the expression of an mRNA encoding the chimeric polypeptide. The promoter may be in any of the expression vectors described herein including those described in Examples 21 and 48.

Preferably, the fusion vector is maintained in multiple copies in each host cell. In some embodiments, the multiple copies are maintained extrachromosomally. In other embodiments, the 30 multiple copies result from amplification of a chromosomal sequence.

The first polypeptide portion may comprise any of the polypeptides encoded by the EST-related nucleic acids, positional segments of EST-related nucleic acids or fragments of positional segments of EST-related nucleic acids. In some embodiments, the first polypeptide portion may be one of the ESTrelated polypeptides, fragments of EST-related polypeptides, positional segments of EST-related 35 polypeptides, or fragments of positional segments of EST-related polypeptides.

The second polypeptide portion may comprise any polypeptide of interest. In some embodiments, the second polypeptide portion may comprise a polypeptide having a detectable enzymatic activity such as green fluorescent protein or β galactosidase. Chimeric polypeptides in which the second polypeptide portion comprises a detectable polypeptide may be used to determine the intracellular localization of the first polypeptide portion. In such procedures, the fusion vector encoding the chimeric polypeptide is introduced into a host cell under conditions which facilitate the expression of

- 5 the chimeric polypeptide. Where appropriate, the cells are treated with a detection reagent which is visible under the microscope following a catalytic reaction with the detectable polypeptide and the cellular location of the detection reagent is determined. For example, if the polypeptide having a detectable enzymatic activity is β galactosidase, the cells may be treated with Xgal. Alternatively, where the detectable polypeptide is directly detectable without the addition of a detection reagent, the
- intracellular location of the chimeric polypeptide is determined by performing microscopy under conditions in which the dectable polypeptide is visible. For example, if the detectable polypeptide is green fluorescent protein or a modified version thereof, microscopy is performed by exposing the host cells to light having an appropriate wavelength to cause the green fluorescent protein or modified version thereof to fluoresce.
- Alternatively, the second polypeptide portion may comprise a polypeptide whose isolation, purification, or enrichment is desired. In such embodiments, the isolation, purification, or enrichment of the second polypeptide portion may be achieved by performing the immunoaffinity chromatography procedures described below using an immunoaffinity column having an antibody directed against the first polypeptide portion coupled thereto.
- The proteins encoded by the EST-related nucleic acids, positional segments of EST-related nucleic acids or fragments of positional segments of EST-related nucleic acids or the EST-related polypeptides, fragments of EST-related polypeptides, positional segments of EST-related polypeptides, or fragments of positional segments of EST-related polypeptides may also be used to generate antibodies as explained herein in order to identify the tissue type or cell species from which a sample is derived as described in Example 50.

EXAMPLE 50

Identification of Tissue Types or Cell Species by Means of Labeled Tissue Specific Antibodies

- Identification of specific tissues is accomplished by the visualization of tissue specific antigens by means of antibody preparations as described herein which are conjugated, directly or indirectly to a detectable marker. Selected labeled antibody species bind to their specific antigen binding partner in tissue sections, cell suspensions, or in extracts of soluble proteins from a tissue sample to provide a pattern for qualitative or semi-qualitative interpretation.
- Antisera for these procedures must have a potency exceeding that of the native preparation, and for that reason, antibodies are concentrated to a mg/ml level by isolation of the gamma globulin fraction, for example, by ion-exchange chromatography or by ammonium sulfate fractionation. Also, to provide

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the most specific antisera, unwanted antibodies, for example to common proteins, must be removed from the gamma globulin fraction, for example by means of insoluble immunoabsorbents, before the antibodies are labeled with the marker. Either monoclonal or heterologous antisera is suitable for either procedure.

5 1. Immunohistochemical Techniques

Purified, high-titer antibodies, prepared as described above, are conjugated to a detectable marker, as described, for example, by Fudenberg, H., Chap. 26 in: *Basic 503 Clinical Immunology*, 3rd Ed. Lange, Los Altos, California (1980) or Rose, *et al.*, Chap. 12 in: *Methods in Immunodiagnosis*, 2d Ed. John Wiley and Sons, New York (1980).

A fluorescent marker, either fluorescein or rhodamine, is preferred, but antibodies can also be labeled with an enzyme that supports a color producing reaction with a substrate, such as horseradish peroxidase. Markers can be added to tissue-bound antibody in a second step, as described below. Alternatively, the specific antitissue antibodies can be labeled with ferritin or other electron dense particles, and localization of the ferritin coupled antigen-antibody complexes achieved by means of an electron microscope. In yet another approach, the antibodies are radiolabeled, with, for example ¹²⁵I, and detected by overlaying the antibody treated preparation with photographic emulsion.

Preparations to carry out the procedures can comprise monoclonal or polyclonal antibodies to a single protein or peptide identified as specific to a tissue type, for example, brain tissue, or antibody preparations to several antigenically distinct tissue specific antigens can be used in panels, independently or in mixtures, as required.

Tissue sections and cell suspensions are prepared for immunohistochemical examination according to common histological techniques. Multiple cryostat sections (about 4 μm, unfixed) of the unknown tissue and known control, are mounted and each slide covered with different dilutions of the antibody preparation. Sections of known and unknown tissues should also be treated with preparations to provide a positive control, a negative control, for example, pre-immune sera, and a control for non-specific staining, for example, buffer.

Treated sections are incubated in a humid chamber for 30 min at room temperature, rinsed, then washed in buffer for 30-45 min. Excess fluid is blotted away, and the marker developed.

If the tissue specific antibody was not labeled in the first incubation, it can be labeled at this time in a second antibody-antibody reaction, for example, by adding fluorescein- or enzyme-conjugated antibody against the immunoglobulin class of the antiserum-producing species, for example, fluorescein labeled antibody to mouse IgG. Such labeled sera are commercially available.

The antigen found in the tissues by the above procedure can be quantified by measuring the intensity of color or fluorescence on the tissue section, and calibrating that signal using appropriate standards.

2. Identification of Tissue Specific Soluble Proteins

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The visualization of tissue specific proteins and identification of unknown tissues from that procedure is carried out using the labeled antibody reagents and detection strategy as described for immunohistochemistry; however the sample is prepared according to an electrophoretic technique to distribute the proteins extracted from the tissue in an orderly array on the basis of molecular weight for 5 detection.

A tissue sample is homogenized using a Virtis apparatus; cell suspensions are disrupted by Dounce homogenization or osmotic lysis, using detergents in either case as required to disrupt cell membranes, as is the practice in the art. Insoluble cell components such as nuclei, microsomes, and membrane fragments are removed by ultracentrifugation, and the soluble protein-containing fraction 10 concentrated if necessary and reserved for analysis.

A sample of the soluble protein solution is resolved into individual protein species by conventional SDS polyacrylamide electrophoresis as described, for example, by Davis, L. et al., Section 19-2 in: Basic Methods in Molecular Biology (P. Leder, ed), Elsevier, New York (1986), using a range of amounts of polyacrylamide in a set of gels to resolve the entire molecular weight range of proteins to 15 be detected in the sample. A size marker is run in parallel for purposes of estimating molecular weights of the constituent proteins. Sample size for analysis is a convenient volume of from 5 to 55 µl, and containing from about 1 to 100 µg protein. An aliquot of each of the resolved proteins is transferred by blotting to a nitrocellulose filter paper, a process that maintains the pattern of resolution. Multiple copies are prepared. The procedure, known as Western Blot Analysis, is well described in Davis, L. et al., 20 supra Section 19-3. One set of nitrocellulose blots is stained with Coomassie Blue dye to visualize the entire set of proteins for comparison with the antibody bound proteins. The remaining nitrocellulose filters are then incubated with a solution of one or more specific antisera to tissue specific proteins prepared as described in Examples 20 and 33. In this procedure, as in procedure A above, appropriate positive and negative sample and reagent controls are run.

In either procedure described above a detectable label can be attached to the primary tissue antigen-primary antibody complex according to various strategies and permutations thereof. In a straightforward approach, the primary specific antibody can be labeled; alternatively, the unlabeled complex can be bound by a labeled secondary anti-IgG antibody. In other approaches, either the primary or secondary antibody is conjugated to a biotin molecule, which can, in a subsequent step, bind an avidin 30 conjugated marker. According to yet another strategy, enzyme labeled or radioactive protein A, which has the property of binding to any IgG, is bound in a final step to either the primary or secondary antibody.

EXAMPLE 51

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Immunohistochemical Localization of Polypeptides

The antibodies prepared as described herein above may be utilized to determine the cellular location of a polypeptide. The polypeptide may be any of the polypeptides encoded by EST-related

nucleic acids, positional segments of EST-related nucleic acids or fragments of positional segments of EST-related nucleic acids or the polypeptide may be one of the EST-related polypeptides, fragments of EST-related polypeptides, positional segments of EST-related polypeptides, or fragments of positional segments of EST-related polypeptides. In some embodiments, the polypeptide may be a chimeric polypeptide such as those encoded by the fusion vectors of Example 49.

Cells expressing the polypeptide to be localized are applied to a microscope slide and fixed using any of the procedures typically employed in immunohistochemical localization techniques, including the methods described in *Current Protocols in Molecular Biology*, John Wiley and Sons, Inc. 1997. Following a washing step, the cells are contacted with the antibody. In some embodiments, the antibody is conjugated to a detectable marker as described above to facilitate detection. Alternatively, in some embodiments, after the cells have been contacted with an antibody to the polypeptide to be localized, a secondary antibody which has been conjugated to a detectable marker is placed in contact with the antibody against the polypeptide to be localized.

Thereafter, microscopy is performed under conditions suitable for visualizing the cellular location of the polypeptide.

The visualization of tissue specific antigen binding at levels above those seen in control tissues to one or more tissue specific antibodies, directed against the polypeptides encoded by EST-related nucleic acids, positional segments of EST-related nucleic acids or fragments of positional segments of EST-related nucleic acids or antibodies against the EST-related polypeptides, fragments of EST-related polypeptides, positional segments of EST-related polypeptides, or fragments of positional segments of EST-related polypeptides, can identify tissues of unknown origin, for example, forensic samples, or differentiated tumor tissue that has metastasized to foreign bodily sites.

The antibodies described herein may also be used in the immunoaffinity chromatography techniques described below to isolate, purify or enrich the polypeptides encoded by the EST-related nucleic acids, positional segments of EST-related nucleic acids or fragments of positional segments of EST-related nucleic acids or to isolate, purify or enrich EST-related polypeptides, fragments of EST-related polypeptides, positional segments of EST-related polypeptides, or fragments of positional segments of EST-related polypeptides. The immunoaffinity chromatography techniques described below may also be used to isolate, purify or enrich polypeptides which have been linked to the polypeptides encoded by the EST-related nucleic acids, positional segments of EST-related nucleic acids or to isolate, purify or enrich polypeptides which have been linked to EST-related polypeptides, fragments of EST-related polypeptides, positional segments of EST-related polypeptides, or fragments of positional segments of EST-related polypeptides, or fragments of positional segments of EST-related polypeptides.

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Immunoaffinity Chromatography

Antibodies prepared as described above are coupled to a support. Preferably, the antibodies are monoclonal antibodies, but polyclonal antibodies may also be used. The support may be any of those typically employed in immunoaffinity chromatography, including Sepharose CL-4B (Pharmacia, Piscataway, NJ), Sepharose CL-2B (Pharmacia, Piscataway, NJ), Affi-gel 10 (Biorad, Richmond, CA), or glass beads.

The antibodies may be coupled to the support using any of the coupling reagents typically used in immunoaffinity chromatography, including cyanogen bromide. After coupling the antibody to the support, the support is contacted with a sample which contains a target polypeptide whose isolation, purification or enrichment is desired. The target polypeptide may be a polypeptide encoded by the EST-related nucleic acids, positional segments of EST-related nucleic acids or fragments of positional segments of EST-related polypeptides, positional segments of EST-related polypeptides, or fragments of positional segments of EST-related polypeptides. The target polypeptides may also be polypeptides which have been linked to the polypeptides encoded by the EST-related nucleic acids, positional segments of EST-related nucleic acids or fragments of positional segments of EST-related nucleic acids or the target polypeptides may be polypeptides which have been linked to EST-related nucleic acids or the target polypeptides may be polypeptides which have been linked to EST-related polypeptides, fragments of EST-related polypeptides, positional segments of EST-related polypeptides, or fragments of positional segments of EST-related polypeptides using the fusion vectors described above.

Preferably, the sample is placed in contact with the support for a sufficient amount of time and under appropriate conditions to allow at least 50% of the target polypeptide to specifically bind to the antibody coupled to the support.

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Thereafter, the support is washed with an appropriate wash solution to remove polypeptides which have non-specifically adhered to the support. The wash solution may be any of those typically employed in immunoaffinity chromatography, including PBS, Tris-lithium chloride buffer (0.1M lysine base and 0.5M lithium chloride, pH 8.0), Tris-hydrochloride buffer (0.05M Tris-hydrochloride, pH 8.0), or Tris/Triton/NaCl buffer (50mM Tris.cl, pH 8.0 or 9.0, 0.1% Triton X-100, and 0.5MNaCl).

After washing, the specifically bound target polypeptide is eluted from the support using the high pH or low pH elution solutions typically employed in immunoaffinity chromatography. In particular, the elution solutions may contain an eluant such as triethanolamine, diethylamine, calcium chloride, sodium thiocyanate, potasssium bromide, acetic acid, or glycine. In some embodiments, the elution solution may also contain a detergent such as Triton X-100 or octyl-β-D-glucoside.

The EST-related nucleic acids, positional segments of EST-related nucleic acids or fragments of positional segments of EST-related nucleic acids may also be used to clone sequences located upstream of the 5'ESTs which are capable of regulating gene expression, including promoter sequences, enhancer

sequences, and other upstream sequences which influence transcription or translation levels. Once identified and cloned, these upstream regulatory sequences may be used in expression vectors designed to direct the expression of an inserted gene in a desired spatial, temporal, developmental, or quantitative fashion. Example 51 describes a method for cloning sequences upstream of the EST-related nucleic acids, positional segments of EST-related nucleic acids or fragments of positional segments of EST-related nucleic acids.

2. Identification of upstream sequences with promoting or regulatory activities

EXAMPLE 53

10 <u>Use of EST-related nucleic acids, positional segments of EST-related nucleic acids or fragments of positional segments of EST-related nucleic acids to Clone Upstream Sequences from Genomic DNA</u>

Sequences derived from EST-related nucleic acids, positional segments of EST-related nucleic acids or fragments of positional segments of EST-related nucleic acids may be used to isolate the promoters of the corresponding genes using chromosome walking techniques. In one chromosome walking technique, which utilizes the GenomeWalkerTM kit available from Clontech, five complete genomic DNA samples are each digested with a different restriction enzyme which has a 6 base recognition site and leaves a blunt end. Following digestion, oligonucleotide adapters are ligated to each end of the resulting genomic DNA fragments.

For each of the five genomic DNA libraries, a first PCR reaction is performed according to the manufacturer's instructions using an outer adapter primer provided in the kit and an outer gene specific primer. The gene specific primer should be selected to be specific for 5' EST of interest and should have a melting temperature, length, and location in the EST-related nucleic acids, positional segments of EST-related nucleic acids or fragments of positional segments of EST-related nucleic acids which is consistent with its use in PCR reactions. Each first PCR reaction contains 5ng of genomic DNA, 5 μl of 10X Tth reaction buffer, 0.2 mM of each dNTP, 0.2 μM each of outer adapter primer and outer gene specific primer, 1.1 mM of Mg(OAc)₂, and 1 μl of the Tth polymerase 50X mix in a total volume of 50 μl. The reaction cycle for the first PCR reaction is as follows: 1 min at 94°C / 2 sec at 94°C, 3 min at 72°C (7 cycles) / 2 sec at 94°C, 3 min at 67°C (32 cycles) / 5 min at 67°C.

The product of the first PCR reaction is diluted and used as a template for a second PCR
reaction according to the manufacturer's instructions using a pair of nested primers which are located internally on the amplicon resulting from the first PCR reaction. For example, 5 μl of the reaction product of the first PCR reaction mixture may be diluted 180 times. Reactions are made in a 50 μl volume having a composition identical to that of the first PCR reaction except the nested primers are used. The first nested primer is specific for the adapter, and is provided with the GenomeWalkerTM
kit. The second nested primer is specific for the particular EST-related nucleic acids, positional segments of EST-related nucleic acids for which the promoter is to be cloned and should have a melting temperature, length, and location in

the EST-related nucleic acids, positional segments of EST-related nucleic acids or fragments of positional segments of EST-related nucleic acids which is consistent with its use in PCR reactions. The reaction parameters of the second PCR reaction are as follows: 1 min at 94°C / 2 sec at 94°C, 3 min at 72°C (6 cycles) / 2 sec at 94°C, 3 min at 67°C (25 cycles) / 5 min at 67°C. The product of the second PCR reaction is purified, cloned, and sequenced using standard techniques.

Alternatively, two or more human genomic DNA libraries can be constructed by using two or more restriction enzymes. The digested genomic DNA is cloned into vectors which can be converted into single stranded, circular, or linear DNA. A biotinylated oligonucleotide comprising at least 10, 12, 15, 18, 20, 23, 25, 27, 30, 35, 40, or 50 nucleotides from the EST-related nucleic acids, positional 10 segments of EST-related nucleic acids or fragments of positional segments of EST-related nucleic acids sequence is hybridized to the single stranded DNA. Hybrids between the biotinylated oligonucleotide and the single stranded DNA containing the EST-related nucleic acids, positional segments of ESTrelated nucleic acids or fragments of positional segments of EST-related nucleic acids are isolated as described above. Thereafter, the single stranded DNA containing the EST-related nucleic acids, 15 positional segments of EST-related nucleic acids or fragments of positional segments of EST-related nucleic acids is released from the beads and converted into double stranded DNA using a primer specific for the EST-related nucleic acids, positional segments of EST-related nucleic acids or fragments of positional segments of EST-related nucleic acids or a primer corresponding to a sequence included in the cloning vector. The resulting double stranded DNA is transformed into bacteria. cDNAs containing the 20 EST-related nucleic acids, positional segments of EST-related nucleic acids or fragments of positional segments of EST-related nucleic acids are identified by colony PCR or colony hybridization.

Once the upstream genomic sequences have been cloned and sequenced as described above, prospective promoters and transcription start sites within the upstream sequences may be identified by comparing the sequences upstream of the EST-related nucleic acids, positional segments of EST-related nucleic acids or fragments of positional segments of EST-related nucleic acids with databases containing known transcription start sites, transcription factor binding sites, or promoter sequences.

In addition, promoters in the upstream sequences may be identified using promoter reporter vectors as described in Example 54.

30 EXAMPLE 54

Identification of Promoters in Cloned Upstream Sequences

The genomic sequences upstream of the EST-related nucleic acids, positional segments of EST-related nucleic acids or fragments of positional segments of EST-related nucleic acids are cloned into a suitable promoter reporter vector, such as the pSEAP-Basic, pSEAP-Enhancer, pβ-gal-Basic, pβ-gal35 Enhancer, or pEGFP-1 Promoter Reporter vectors available from Clontech. Briefly, each of these promoter reporter vectors include multiple cloning sites positioned upstream of a reporter gene encoding a readily assayable protein such as secreted alkaline phosphatase, β-galactosidase, or green fluorescent

protein. The sequences upstream of the EST-related nucleic acids, positional segments of EST-related nucleic acids or fragments of positional segments of EST-related nucleic acids are inserted into the cloning sites upstream of the reporter gene in both orientations and introduced into an appropriate host cell. The level of reporter protein is assayed and compared to the level obtained from a vector which lacks an insert in the cloning site. The presence of an elevated expression level in the vector containing the insert with respect to the control vector indicates the presence of a promoter in the insert. If necessary, the upstream sequences can be cloned into vectors which contain an enhancer for augmenting transcription levels from weak promoter sequences. A significant level of expression above that observed with the vector lacking an insert indicates that a promoter sequence is present in the inserted upstream sequence.

Appropriate host cells for the promoter reporter vectors may be chosen based on the results of the above described determination of expression patterns of the EST-related nucleic acids, positional segments of EST-related nucleic acids or fragments of positional segments of EST-related nucleic acids. For example, if the expression pattern analysis indicates that the mRNA corresponding to a particular EST-related nucleic acids, positional segments of EST-related nucleic acids or fragments of positional segments of EST-related nucleic acids is expressed in fibroblasts, the promoter reporter vector may be introduced into a human fibroblast cell line.

Promoter sequences within the upstream genomic DNA may be further defined by constructing nested deletions in the upstream DNA using conventional techniques such as Exonuclease III digestion.

The resulting deletion fragments can be inserted into the promoter reporter vector to determine whether the deletion has reduced or obliterated promoter activity. In this way, the boundaries of the promoters may be defined. If desired, potential individual regulatory sites within the promoter may be identified using site directed mutagenesis or linker scanning to obliterate potential transcription factor binding sites within the promoter individually or in combination. The effects of these mutations on transcription levels may be determined by inserting the mutations into the cloning sites in the promoter reporter vectors.

EXAMPLE 55

Cloning and Identification of Promoters

30 Using the method described in Example 54 above with 5' ESTs, sequences upstream of several genes were obtained. Using the primer pairs GGG AAG ATG GAG ATA GTA TTG CCT G (SEQ ID NO:15) and CTG CCA TGT ACA TGA TAG AGA GAT TC (SEQ ID NO:16), the promoter having the internal designation P13H2 (SEQ ID NO:17) was obtained.

Using the primer pairs GTA CCA GGGG ACT GTG ACC ATT GC (SEQ ID NO:18) and CTG

TGA CCA TTG CTC CCA AGA GAG (SEQ ID NO:19), the promoter having the internal designation

P15B4 (SEQ ID NO:20) was obtained.

Using the primer pairs CTG GGA TGG AAG GCA CGG TA (SEQ ID NO:21) and GAG ACC ACA CAG CTA GAC AA (SEQ ID NO:22), the promoter having the internal designation P29B6 (SEQ ID NO:23) was obtained.

Figure 4 provides a schematic description of the promoters isolated and the way they are

seembled with the corresponding 5' tags. The upstream sequences were screened for the presence of
motifs resembling transcription factor binding sites or known transcription start sites using the computer
program MatInspector release 2.0, August 1996.

Figure 5 describes the transcription factor binding sites present in each of these promoters. The columns labeled matrice provides the name of the MatInspector matrix used. The column labeled position provides the 5' position of the promoter site. Numeration of the sequence starts from the transcription site as determined by matching the genomic sequence with the 5' EST sequence. The column labeled "orientation" indicates the DNA strand on which the site is found, with the + strand being the coding strand as determined by matching the genomic sequence with the sequence of the 5' EST. The column labeled "score" provides the MatInspector score found for this site. The column labeled "length" provides the length of the site in nucleotides. The column labeled "sequence" provides the sequence of the site found.

Bacterial clones containing plasmids containing the promoter sequences described above described above are presently stored in the inventor's laboratories under the internal identification numbers provided above. The inserts may be recovered from the deposited materials by growing an aliquot of the appropriate bacterial clone in the appropriate medium. The plasmid DNA can then be isolated using plasmid isolation procedures familiar to those skilled in the art such as alkaline lysis minipreps or large scale alkaline lysis plasmid isolation procedures. If desired the plasmid DNA may be further enriched by centrifugation on a cesium chloride gradient, size exclusion chromatography, or anion exchange chromatography. The plasmid DNA obtained using these procedures may then be manipulated using standard cloning techniques familiar to those skilled in the art. Alternatively, a PCR can be done with primers designed at both ends of the inserted EST-related nucleic acids, positional segments of EST-related nucleic acids or fragments of positional segments of EST-related nucleic acids. The PCR product which corresponds to the EST-related nucleic acids, positional segments of EST-related nucleic acids can then be manipulated using standard cloning techniques familiar to those skilled in the art.

The promoters and other regulatory sequences located upstream of the EST-related nucleic acids, positional segments of EST-related nucleic acids or fragments of positional segments of EST-related nucleic acids may be used to design expression vectors capable of directing the expression of an inserted gene in a desired spatial, temporal, developmental, or quantitative manner. A promoter capable of directing the desired spatial, temporal, developmental, and quantitative patterns may be selected using the results of the expression analysis described above. For example, if a promoter which confers a high level of expression in muscle is desired, the promoter sequence upstream of EST-related nucleic acids,

positional segments of EST-related nucleic acids or fragments of positional segments of EST-related nucleic acids derived from an mRNA which are expressed at a high level in muscle, as determined by the methods above, may be used in the expression vector.

Preferably, the desired promoter is placed near multiple restriction sites to facilitate the cloning of the desired insert downstream of the promoter, such that the promoter is able to drive expression of the inserted gene. The promoter may be inserted in conventional nucleic acid backbones designed for extrachromosomal replication, integration into the host chromosomes or transient expression. Suitable backbones for the present expression vectors include retroviral backbones, backbones from eukaryotic episomes such as SV40 or Bovine Papilloma Virus, backbones from bacterial episomes, or artificial chromosomes.

Preferably, the expression vectors also include a polyA signal downstream of the multiple restriction sites for directing the polyadenylation of mRNA transcribed from the gene inserted into the expression vector.

Following the identification of promoter sequences, proteins which interact with the promoter may be identified as described in Example 56 below.

EXAMPLE 56

Identification of Proteins Which Interact with

Promoter Sequences, Upstream Regulatory Sequences, or mRNA

Sequences within the promoter region which are likely to bind transcription factors may be identified by homology to known transcription factor binding sites or through conventional mutagenesis or deletion analyses of reporter plasmids containing the promoter sequence. For example, deletions may be made in a reporter plasmid containing the promoter sequence of interest operably linked to an assayable reporter gene. The reporter plasmids carrying various deletions within the promoter region are transfected into an appropriate host cell and the effects of the deletions on expression levels is assessed. Transcription factor binding sites within the regions in which deletions reduce expression levels may be further localized using site directed mutagenesis, linker scanning analysis, or other techniques familiar to those skilled in the art.

Nucleic acids encoding proteins which interact with sequences in the promoter may be identified using one-hybrid systems such as those described in the manual accompanying the Matchmaker One-Hybrid System kit available from Clontech (Catalog No. K1603-1). Briefly, the Matchmaker One-hybrid system is used as follows. The target sequence for which it is desired to identify binding proteins is cloned upstream of a selectable reporter gene and integrated into the yeast genome. Preferably, multiple copies of the target sequences are inserted into the reporter plasmid in tandem. A library comprised of fusions between cDNAs to be evaluated for the ability to bind to the promoter and the activation domain of a yeast transcription factor, such as GAL4, is transformed into the yeast strain containing the integrated reporter sequence. The yeast are plated on selective media to select cells

expressing the selectable marker linked to the promoter sequence. The colonies which grow on the selective media contain genes encoding proteins which bind the target sequence. The inserts in the genes encoding the fusion proteins are further characterized by sequencing. In addition, the inserts may be inserted into expression vectors or in vitro transcription vectors. Binding of the polypeptides encoded by 5 the inserts to the promoter DNA may be confirmed by techniques familiar to those skilled in the art, such as gel shift analysis or DNAse protection analysis.

VIII. Use of EST-related nucleic acids, positional segments of EST-related nucleic acids or fragments of positional segments of EST-related nucleic acids in Gene Therapy

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The present invention also comprises the use of EST-related nucleic acids, positional segments of EST-related nucleic acids or fragments of positional segments of EST-related nucleic acids in gene therapy strategies, including antisense and triple helix strategies as described in Examples 57 and 58 below. In antisense approaches, nucleic acid sequences complementary to an mRNA are hybridized to the mRNA intracellularly, thereby blocking the expression of the protein encoded by the mRNA. The 15 antisense sequences may prevent gene expression through a variety of mechanisms. For example, the antisense sequences may inhibit the ability of ribosomes to translate the mRNA. Alternatively, the antisense sequences may block transport of the mRNA from the nucleus to the cytoplasm, thereby limiting the amount of mRNA available for translation. Another mechanism through which antisense sequences may inhibit gene expression is by interfering with mRNA splicing. In yet another strategy, 20 the antisense nucleic acid may be incorporated in a ribozyme capable of specifically cleaving the target mRNA.

EXAMPLE 57

Preparation and Use of Antisense Oligonucleotides

25 The antisense nucleic acid molecules to be used in gene therapy may be either DNA or RNA sequences. They may comprise a sequence complementary to the sequence of the EST-related nucleic acids, positional segments of EST-related nucleic acids or fragments of positional segments of ESTrelated nucleic acids. The antisense nucleic acids should have a length and melting temperature sufficient to permit formation of an intracellular duplex with sufficient stability to inhibit the expression 30 of the mRNA in the duplex. Strategies for designing antisense nucleic acids suitable for use in gene therapy are disclosed in Green et al., Ann. Rev. Biochem. 55:569-597 (1986) and Izant and Weintraub, Cell 36:1007-1015 (1984).

In some strategies, antisense molecules are obtained from a nucleotide sequence encoding a protein by reversing the orientation of the coding region with respect to a promoter so as to transcribe the 35 opposite strand from that which is normally transcribed in the cell. The antisense molecules may be transcribed using in vitro transcription systems such as those which employ T7 or SP6 polymerase to

generate the transcript. Another approach involves transcription of the antisense nucleic acids *in vivo* by operably linking DNA containing the antisense sequence to a promoter in an expression vector.

Alternatively, oligonucleotides which are complementary to the strand normally transcribed in the cell may be synthesized *in vitro*. Thus, the antisense nucleic acids are complementary to the corresponding mRNA and are capable of hybridizing to the mRNA to create a duplex. In some embodiments, the antisense sequences may contain modified sugar phosphate backbones to increase stability and make them less sensitive to RNase activity. Examples of modifications suitable for use in antisense strategies are described by Rossi *et al.*, *Pharmacol. Ther.* 50(2):245-254, (1991).

Various types of antisense oligonucleotides complementary to the sequence of the EST-related nucleic acids, positional segments of EST-related nucleic acids or fragments of positional segments of EST-related nucleic acids may be used. In one preferred embodiment, stable and semi-stable antisense oligonucleotides described in International Application No. PCT WO94/23026 are used. In these molecules, the 3' end or both the 3' and 5' ends are engaged in intramolecular hydrogen bonding between complementary base pairs. These molecules are better able to withstand exonuclease attacks and exhibit increased stability compared to conventional antisense oligonucleotides.

In another preferred embodiment, the antisense oligodeoxynucleotides against herpes simplex virus types 1 and 2 described in International Application No. WO 95/04141 are used.

In yet another preferred embodiment, the covalently cross-linked antisense oligonucleotides described in International Application No. WO 96/31523 are used. These double- or single-stranded oligonucleotides comprise one or more, respectively, inter- or intra-oligonucleotide covalent cross-linkages, wherein the linkage consists of an amide bond between a primary amine group of one strand and a carboxyl group of the other strand or of the same strand, respectively, the primary amine group being directly substituted in the 2' position of the strand nucleotide monosaccharide ring, and the carboxyl group being carried by an aliphatic spacer group substituted on a nucleotide or nucleotide analog of the other strand or the same strand, respectively.

The antisense oligodeoxynucleotides and oligonucleotides disclosed in International Application No. WO 92/18522 may also be used. These molecules are stable to degradation and contain at least one transcription control recognition sequence which binds to control proteins and are effective as decoys therefor. These molecules may contain "hairpin" structures, "dumbbell" structures, "modified dumbbell" structures, "cross-linked" decoy structures and "loop" structures.

In another preferred embodiment, the cyclic double-stranded oligonucleotides described in European Patent Application No. 0 572 287 A2. These ligated oligonucleotide "dumbbells" contain the binding site for a transcription factor and inhibit expression of the gene under control of the transcription factor by sequestering the factor.

Use of the closed antisense oligonucleotides disclosed in International Application No. WO 92/19732 is also contemplated. Because these molecules have no free ends, they are more resistant to

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degradation by exonucleases than are conventional oligonucleotides. These oligonucleotides may be multifunctional, interacting with several regions which are not adjacent to the target mRNA.

The appropriate level of antisense nucleic acids required to inhibit gene expression may be determined using *in vitro* expression analysis. The antisense molecule may be introduced into the cells by diffusion, injection, infection or transfection using procedures known in the art. For example, the antisense nucleic acids can be introduced into the body as a bare or naked oligonucleotide, oligonucleotide encapsulated in lipid, oligonucleotide sequence encapsidated by viral protein, or as an oligonucleotide operably linked to a promoter contained in an expression vector. The expression vector may be any of a variety of expression vectors known in the art, including retroviral or viral vectors, vectors capable of extrachromosomal replication, or integrating vectors. The vectors may be DNA or RNA.

The antisense molecules are introduced onto cell samples at a number of different concentrations preferably between 1x10⁻¹⁰M to 1x10⁻⁴M. Once the minimum concentration that can adequately control gene expression is identified, the optimized dose is translated into a dosage suitable for use *in vivo*. For example, an inhibiting concentration in culture of 1x10⁻⁷ translates into a dose of approximately 0.6 mg/kg bodyweight. Levels of oligonucleotide approaching 100 mg/kg bodyweight or higher may be possible after testing the toxicity of the oligonucleotide in laboratory animals. It is additionally contemplated that cells from the vertebrate are removed, treated with the antisense oligonucleotide, and reintroduced into the vertebrate.

It is further contemplated that the antisense oligonucleotide sequence is incorporated into a ribozyme sequence to enable the antisense to specifically bind and cleave its target mRNA. For technical applications of ribozyme and antisense oligonucleotides see Rossi *et al.*, *supra*.

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In a preferred application of this invention, the polypeptide encoded by the gene is first identified, so that the effectiveness of antisense inhibition on translation can be monitored using techniques that include but are not limited to antibody-mediated tests such as RIAs and ELISA, functional assays, or radiolabeling.

The EST-related nucleic acids, positional segments of EST-related nucleic acids or fragments of positional segments of EST-related nucleic acids may also be used in gene therapy approaches based on intracellular triple helix formation. Triple helix oligonucleotides are used to inhibit transcription from a genome. They are particularly useful for studying alterations in cell activity as it is associated with a particular gene. The EST-related nucleic acids, positional segments of EST-related nucleic acids or fragments of positional segments of EST-related nucleic acids of the present invention or, more preferably, a portion of those sequences, can be used to inhibit gene expression in individuals having diseases associated with expression of a particular gene. Similarly, the EST-related nucleic acids, positional segments of EST-related nucleic acids or fragments of positional segments of EST-related nucleic acids or fragments of positional segments of EST-related nucleic acids or fragments of positional segments of EST-related nucleic acids can be used to study the effect of inhibiting transcription of a particular gene within a cell. Traditionally, homopurine sequences were considered the most useful for triple helix strategies.

However, homopyrimidine sequences can also inhibit gene expression. Such homopyrimidine oligonucleotides bind to the major groove at homopurine:homopyrimidine sequences. Thus, both types of sequences from the EST-related nucleic acids, positional segments of EST-related nucleic acids or fragments of positional segments of EST-related nucleic acids are contemplated within the scope of this invention.

EXAMPLE 58

Preparation and use of Triple Helix Probes

The sequences of the EST-related nucleic acids, positional segments of EST-related nucleic

acids or fragments of positional segments of EST-related nucleic acids are scanned to identify 10-mer to

20-mer homopyrimidine or homopurine stretches which could be used in triple-helix based strategies for
inhibiting gene expression. Following identification of candidate homopyrimidine or homopurine
stretches, their efficiency in inhibiting gene expression is assessed by introducing varying amounts of
oligonucleotides containing the candidate sequences into tissue culture cells which normally express the
target gene. The oligonucleotides may be prepared on an oligonucleotide synthesizer or they may be
purchased commercially from a company specializing in custom oligonucleotide synthesis, such as
GENSET, Paris, France.

The oligonucleotides may be introduced into the cells using a variety of methods known to those skilled in the art, including but not limited to calcium phosphate precipitation, DEAE-Dextran,

20 electroporation, liposome-mediated transfection or native uptake.

Treated cells are monitored for altered cell function or reduced gene expression using techniques such as Northern blotting, RNase protection assays, or PCR based strategies to monitor the transcription levels of the target gene in cells which have been treated with the oligonucleotide. The cell functions to be monitored are predicted based upon the homologies of the target genes corresponding to the EST-related nucleic acids, positional segments of EST-related nucleic acids or fragments of positional segments of EST-related nucleic acids from which the oligonucleotide were derived with known gene sequences that have been associated with a particular function. The cell functions can also be predicted based on the presence of abnormal physiologies within cells derived from individuals with a particular inherited disease, particularly when the EST-related nucleic acids, positional segments of EST-related nucleic acids or fragments of positional segments of EST-related nucleic acids are associated with the disease using techniques described herein.

The oligonucleotides which are effective in inhibiting gene expression in tissue culture cells may then be introduced *in vivo* using the techniques described above and in Example 56 at a dosage calculated based on the *in vitro* results, as described in Example 57.

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In some embodiments, the natural (beta) anomers of the oligonucleotide units can be replaced with alpha anomers to render the oligonucleotide more resistant to nucleases. Further, an intercalating agent such as ethidium bromide, or the like, can be attached to the 3' end of the alpha oligonucleotide to

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stabilize the triple helix. For information on the generation of oligonucleotides suitable for triple helix formation see Griffin *et al.* (*Science* 245:967-971 (1989)).

EXAMPLE 59

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Use of EST-related nucleic acids, positional segments of

EST-related nucleic acids or fragments of positional segments of

EST-related nucleic acids to express an Encoded Protein in a Host Organism

The EST-related nucleic acids, positional segments of EST-related nucleic acids or fragments of positional segments of EST-related nucleic acids may also be used to express an encoded protein or polypeptide in a host organism to produce a beneficial effect. In addition, nucleic acids encoding the EST-related polypeptides, positional segments of EST-related polypeptides or fragments of positional segments of EST-related polypeptides may be used to express the encoded protein or polypeptide in a host organism to produce a beneficial effect.

In such procedures, the encoded protein or polypeptide may be transiently expressed in the host organism or stably expressed in the host organism. The encoded protein or polypeptide may have any of the activities described above. The encoded protein or polypeptide may be a protein or polypeptide which the host organism lacks or, alternatively, the encoded protein may augment the existing levels of the protein in the host organism.

In some embodiments in which the protein or polypeptide is secreted, nucleic acids encoding the full length protein (i.e. the signal peptide and the mature protein), or nucleic acids encoding only the mature protein (i.e. the protein generated when the signal peptide is cleaved off) is introduced into the host organism.

The nucleic acids encoding the proteins or polypeptides may be introduced into the host organism using a variety of techniques known to those of skill in the art. For example, the extended cDNA may be injected into the host organism as naked DNA such that the encoded protein is expressed in the host organism, thereby producing a beneficial effect.

Alternatively, the nucleic acids encoding the protein or polypeptide may be cloned into an expression vector downstream of a promoter which is active in the host organism. The expression vector may be any of the expression vectors designed for use in gene therapy, including viral or retroviral vectors. The expression vector may be directly introduced into the host organism such that the encoded protein is expressed in the host organism to produce a beneficial effect. In another approach, the expression vector may be introduced into cells *in vitro*. Cells containing the expression vector are thereafter selected and introduced into the host organism, where they express the encoded protein or polypeptide to produce a beneficial effect.

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EXAMPLE 60

The short core hydrophobic region (h) of signal peptides encoded by the sequences of SEQ ID NOs. 24-728 and 766-792 may also be used as a carrier to import a peptide or a protein of interest, socalled cargo, into tissue culture cells (Lin et al., J. Biol. Chem., 270: 14225-14258 (1995); Du et al., J. Peptide Res., 51: 235-243 (1998); Rojas et al., Nature Biotech., 16: 370-375 (1998)).

When cell permeable peptides of limited size (approximately up to 25 amino acids) are to be translocated across cell membrane, chemical synthesis may be used in order to add the h region to either the C-terminus or the N-terminus to the cargo peptide of interest. Alternatively, when longer peptides or proteins are to be imported into cells, nucleic acids can be genetically engineered, using techniques familiar to those skilled in the art, in order to link the extended cDNA sequence encoding the h region to 10 the 5' or the 3' end of a DNA sequence coding for a cargo polypeptide. Such genetically engineered nucleic acids are then translated either in vitro or in vivo after transfection into appropriate cells, using conventional techniques to produce the resulting cell permeable polypeptide. Suitable hosts cells are then simply incubated with the cell permeable polypeptide which is then translocated across the membrane.

This method may be applied to study diverse intracellular functions and cellular processes. For instance, it has been used to probe functionally relevant domains of intracellular proteins and to examine protein-protein interactions involved in signal transduction pathways (Lin et al., supra; Lin et al., J. Biol. Chem., 271: 5305-5308 (1996); Rojas et al., J. Biol. Chem., 271: 27456-27461 (1996); Liu et al., Proc. Natl. Acad. Sci. USA, 93: 11819-11824 (1996); Rojas et al., Bioch. Biophys. Res. Commun., 234: 675-20 680 (1997)).

Such techniques may be used in cellular therapy to import proteins producing therapeutic effects. For instance, cells isolated from a patient may be treated with imported therapeutic proteins and then re-introduced into the host organism.

Alternatively, the h region of signal peptides of the present invention could be used in 25 combination with a nuclear localization signal to deliver nucleic acids into cell nucleus. Such oligonucleotides may be antisense oligonucleotides or oligonucleotides designed to form triple helixes, as describedabove, in order to inhibit processing and maturation of a target cellular RNA.

EXAMPLE 61

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Computer Embodiments

As used herein the term "nucleic acid codes of SEQ ID NOs. 24-811 and 1600-1622" encompasses the nucleotide sequences of SEQ ID NOs. 24-811 and 1600-1622, fragments of SEQ ID NOs. 24-811 and 1600-1622, nucleotide sequences homologous to SEQ ID NOs. 24-811 and 1600-1622 or homologous to fragments of SEQ ID NOs. 24-811 and 1600-1622, and sequences 35 complementary to all of the preceding sequences. The fragments include portions of SEO ID NOs. 24-811 and 1600-1622 comprising at least 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, 150, 200, 300, 400, or 500 consecutive nucleotides of SEQ ID NOs. 24-811 and 1600-1622. Preferably, the fragments are novel

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fragments. Preferably the fragments include polynucleotides described in Table II, polynucleotides described in Table III, polynucleotides described in Table IV or portions thereof comprising at least 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, 150, 200, 300, 400, or 500 consecutive nucleotides of the polynucleotides described in Tables II, III, or IV. Homologous sequences and fragments of SEQ ID 5 NOs. 24-811 and 1600-1622 refer to a sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, 80%, or 75% homology to these sequences. Homology may be determined using any of the computer programs and parameters described in Example 18, including BLAST2N with the default parameters or with any modified parameters. Homologous sequences also include RNA sequences in which uridines replace the thymines in the nucleic acid codes of SEQ ID NOs. 24-811 and 1600-1622. The 10 homologous sequences may be obtained using any of the procedures described herein or may result from the correction of a sequencing error as described above. Preferably the homologous sequences and fragments of SEQ ID NOs. 24-811 and 1600-1622 include polynucleotides described in Table II, polynucleotides described in Table III, polynucleotides described in Table IV or portions thereof comprising at least 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, 150, 200, 300, 400, or 500 consecutive 15 nucleotides of the polynucleotides described in Tables II, III, or IV. It will be appreciated that the nucleic acid codes of SEQ ID NOs. 24-811 and 1600-1622 can be represented in the traditional single character format (See the inside back cover of Styer, Lubert. Biochemistry, 3rd edition. W. H Freeman & Co., New York.) or in any other format which records the identity of the nucleotides in a sequence.

As used herein the term "polypeptide codes of SEQ ID NOS. 812-1599" encompasses the 20 polypeptide sequence of SEQ ID NOs. 812-1599 which are encoded by the 5' EST s of SEQ ID NOs. 24-811 and 1600-1622, polypeptide sequences homologous to the polypeptides of SEQ ID NOS. 812-1599, or fragments of any of the preceding sequences. Homologous polypeptide sequences refer to a polypeptide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, 80%, 75% homology to one of the polypeptide sequences of SEQ ID NOS. 812-1599. Homology may be determined using any 25 of the computer programs and parameters described herein, including FASTA with the default parameters or with any modified parameters. The homologous sequences may be obtained using any of the procedures described herein or may result from the correction of a sequencing error as described above. The polypeptide fragments comprise at least 5, 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, or 150 consecutive amino acids of the polypeptides of SEQ ID NOS. 812-1599. Preferably, the fragments are 30 novel fragments. Preferably, the fragments include polypeptides encoded by the polynucleotides described in Table II, or portions thereof comprising at least 5, 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, or 150 consecutive amino acids of the polypeptides encoded by the polynucleotides described in Table II. It will be appreciated that the polypeptide codes of the SEQ ID NOS. 812-1599 can be represented in the traditional single character format or three letter format (See the inside back cover of Starrier, Lubert. 35 Biochemistry, 3rd edition. W. H Freeman & Co., New York.) or in any other format which relates the identity of the polypeptides in a sequence.

It will be appreciated by those skilled in the art that the nucleic acid codes of SEQ ID NOs. 24-811 and 1600-1622 and polypeptide codes of SEQ ID NOS. 812-1599 can be stored, recorded, and manipulated on any medium which can be read and accessed by a computer. As used herein, the words "recorded" and "stored" refer to a process for storing information on a computer medium. A skilled artisan can readily adopt any of the presently known methods for recording information on a computer readable medium to generate manufactures comprising one or more of the nucleic acid codes of SEQ ID NOs. 24-811 and 1600-1622, one or more of the polypeptide codes of SEQ ID NOS. 812-1599. Another aspect of the present invention is a computer readable medium having recorded thereon at least 2, 5, 10, 15, 20, 25, 30, or 50 nucleic acid codes of SEQ ID NOs. 812-1599.

Computer readable media include magnetically readable media, optically readable media, electronically readable media and magnetic/optical media. For example, the computer readable media may be a hard disk, a floppy disk, a magnetic tape, CD-ROM, Digital Versatile Disk (DVD), Random
15 Access Memory (RAM), or Read Only Memory (ROM) as well as other types of other media known to those skilled in the art.

Embodiments of the present invention include systems, particularly computer systems which store and manipulate the sequence information described herein. One example of a computer system 100 is illustrated in block diagram form in Figure 6. As used herein, "a computer system" refers to the hardware components, software components, and data storage components used to analyze the nucleotide sequences of the nucleic acid codes of SEQ ID NOs. 24-811 and 1600-1622, or the amino acid sequences of the polypeptide codes of SEQ ID NOS. 812-1599. In one embodiment, the computer system 100 is a Sun Enterprise 1000 server (Sun Microsystems, Palo Alto, CA). The computer system 100 preferably includes a processor for processing, accessing and manipulating the sequence data. The 25 processor 105 can be any well-known type of central processing unit, such as the Pentium III from Intel Corporation, or similar processor from Sun, Motorola, Compaq or International Business Machines.

Preferably, the computer system 100 is a general purpose system that comprises the processor 105 and one or more internal data storage components 110 for storing data, and one or more data retrieving devices for retrieving the data stored on the data storage components. A skilled artisan can readily appreciate that any one of the currently available computer systems are suitable.

In one particular embodiment, the computer system 100 includes a processor 105 connected to a bus which is connected to a main memory 115 (preferably implemented as RAM) and one or more internal data storage devices 110, such as a hard drive and/or other computer readable media having data recorded thereon. In some embodiments, the computer system 100 further includes one or more data retrieving device 118 for reading the data stored on the internal data storage devices 110.

The data retrieving device 118 may represent, for example, a floppy disk drive, a compact disk drive, a magnetic tape drive, etc. In some embodiments, the internal data storage device 110 is a

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removable computer readable medium such as a floppy disk, a compact disk, a magnetic tape, etc. containing control logic and/or data recorded thereon. The computer system 100 may advantageously include or be programmed by appropriate software for reading the control logic and/or the data from the data storage component once inserted in the data retrieving device.

The computer system 100 includes a display 120 which is used to display output to a computer user. It should also be noted that the computer system 100 can be linked to other computer systems 125a-c in a network or wide area network to provide centralized access to the computer system 100.

Software for accessing and processing the nucleotide sequences of the nucleic acid codes of SEQ ID NOs. 24-811 and 1600-1622, or the amino acid sequences of the polypeptide codes of SEQ ID NOS. 812-1599 (such as search tools, compare tools, and modeling tools etc.) may reside in main memory 115 during execution.

In some embodiments, the computer system 100 may further comprise a sequence comparer for comparing the above-described nucleic acid codes of SEQ ID NOs. 24-811 and 1600-1622 or polypeptide codes of SEQ ID NOS. 812-1599 stored on a computer readable medium to reference nucleotide or polypeptide sequences stored on a computer readable medium. A "sequence comparer" refers to one or more programs which are implemented on the computer system 100 to compare a nucleotide or polypeptide sequence with other nucleotide or polypeptide sequences and/or compounds including but not limited to peptides, peptidomimetics, and chemicals stored within the data storage means. For example, the sequence comparer may compare the nucleotide sequences of the nucleic acid codes of SEQ ID NOs. 24-811 and 1600-1622, or the amino acid sequences of the polypeptide codes of SEQ ID NOS. 812-1599 stored on a computer readable medium to reference sequences stored on a computer readable medium to identify homologies, motifs implicated in biological function, or structural motifs. The various sequence comparer programs identified elsewhere in this patent specification are particularly contemplated for use in this aspect of the invention.

Figure 7 is a flow diagram illustrating one embodiment of a process 200 for comparing a new nucleotide or protein sequence with a database of sequences in order to determine the homology levels between the new sequence and the sequences in the database. The database of sequences can be a private database stored within the computer system 100, or a public database such as GENBANK, PIR OR SWISSPROT that is available through the Internet.

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The process 200 begins at a start state 201 and then moves to a state 202 wherein the new sequence to be compared is stored to a memory in a computer system 100. As discussed above, the memory could be any type of memory, including RAM or an internal storage device.

The process 200 then moves to a state 204 wherein a database of sequences is opened for analysis and comparison. The process 200 then moves to a state 206 wherein the first sequence stored in the database is read into a memory on the computer. A comparison is then performed at a state 210 to determine if the first sequence is the same as the second sequence. It is important to note that this step is not limited to performing an exact comparison between the new sequence and the first sequence in the

database. Well-known methods are known to those of skill in the art for comparing two nucleotide or protein sequences, even if they are not identical. For example, gaps can be introduced into one sequence in order to raise the homology level between the two tested sequences. The parameters that control whether gaps or other features are introduced into a sequence during comparison are normally entered by 5 the user of the computer system.

Once a comparison of the two sequences has been performed at the state 210, a determination is made at a decision state 210 whether the two sequences are the same. Of course, the term "same" is not limited to sequences that are absolutely identical. Sequences that are within the homology parameters entered by the user will be marked as "same" in the process 200.

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If a determination is made that the two sequences are the same, the process 200 moves to a state 214 wherein the name of the sequence from the database is displayed to the user. This state notifies the user that the sequence with the displayed name fulfills the homology constraints that were entered. Once the name of the stored sequence is displayed to the user, the process 200 moves to a decision state 218 wherein a determination is made whether more sequences exist in the database. If no more sequences 15 exist in the database, then the process 200 terminates at an end state 220. However, if more sequences do exist in the database, then the process 200 moves to a state 224 wherein a pointer is moved to the next sequence in the database so that it can be compared to the new sequence. In this manner, the new sequence is aligned and compared with every sequence in the database.

It should be noted that if a determination had been made at the decision state 212 that the 20 sequences were not homologous, then the process 200 would move immediately to the decision state 218 in order to determine if any other sequences were available in the database for comparison.

Accordingly, one aspect of the present invention is a computer system comprising a processor, a data storage device having stored thereon a nucleic acid code of SEQ ID NOs. 24-811 and 1600-1622 or a polypeptide code of SEQ ID NOS. 812-1599, a data storage device having 25 retrievably stored thereon reference nucleotide sequences or polypeptide sequences to be compared to the nucleic acid code of SEQ ID NOs. 24-811 and 1600-1622 or polypeptide code of SEQ ID NOS. 812-1599 and a sequence comparer for conducting the comparison. The sequence comparer may indicate a homology level between the sequences compared or identify structural motifs in the above described nucleic acid code of SEQ ID NOs. 24-811 and 1600-1622 and polypeptide codes of 30 SEQ ID NOS. 812-1599 or it may identify structural motifs in sequences which are compared to these nucleic acid codes and polypeptide codes. In some embodiments, the data storage device may have stored thereon the sequences of at least 2, 5, 10, 15, 20, 25, 30, or 50 of the nucleic acid codes of SEQ ID NOs. 24-811 and 1600-1622 or polypeptide codes of SEQ ID NOS. 812-1599.

Another aspect of the present invention is a method for determining the level of homology 35 between a nucleic acid code of SEQ ID NOs. 24-811 and 1600-1622 and a reference nucleotide sequence, comprising the steps of reading the nucleic acid code and the reference nucleotide sequence through the use of a computer program which determines homology levels and determining homology

between the nucleic acid code and the reference nucleotide sequence with the computer program. The computer program may be any of a number of computer programs for determining homology levels, including those specifically enumerated herein, including BLAST2N with the default parameters or with any modified parameters. The method may be implemented using the computer systems described 5 above. The method may also be performed by reading 2, 5, 10, 15, 20, 25, 30, or 50 of the above described nucleic acid codes of SEQ ID NOs. 24-811 and 1600-1622 through use of the computer program and determining homology between the nucleic acid codes and reference nucleotide sequences.

Figure 8 is a flow diagram illustrating one embodiment of a process 250 in a computer for 10 determining whether two sequences are homologous. The process 250 begins at a start state 252 and then moves to a state 254 wherein a first sequence to be compared is stored to a memory. The second sequence to be compared is then stored to a memory at a state 256. The process 250 then moves to a state 260 wherein the first character in the first sequence is read and then to a state 262 wherein the first character of the second sequence is read. It should be understood that if the 15 sequence is a nucleotide sequence, then the character would normally be either A, T, C, G or U. If the sequence is a protein sequence, then it should be in the single letter amino acid code so that the first and sequence sequences can be easily compared.

A determination is then made at a decision state 264 whether the two characters are the same. If they are the same, then the process 250 moves to a state 268 wherein the next characters in the first 20 and second sequences are read. A determination is then made whether the next characters are the same. If they are, then the process 250 continues this loop until two characters are not the same. If a determination is made that the next two characters are not the same, the process 250 moves to a decision state 274 to determine whether there are any more characters either sequence to read.

If there aren't any more characters to read, then the process 250 moves to a state 276 wherein 25 the level of homology between the first and second sequences is displayed to the user. The level of homology is determined by calculating the proportion of characters between the sequences that were the same out of the total number of sequences in the first sequence. Thus, if every character in a first 100 nucleotide sequence aligned with a every character in a second sequence, the homology level would be 100%.

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Alternatively, the computer program may be a computer program which compares the nucleotide sequences of the nucleic acid codes of the present invention, to reference nucleotide sequences in order to determine whether the nucleic acid code of SEQ ID NOs. 24-811 and 1600-1622 differs from a reference nucleic acid sequence at one or more positions. Optionally such a program records the length and identity of inserted, deleted or substituted nucleotides with respect to the sequence 35 of either the reference polynucleotide or the nucleic acid code of SEQ ID NOs. 24-811 and 1600-1622. In one embodiment, the computer program may be a program which determines whether the nucleotide sequences of the nucleic acid codes of SEQ ID NOs. 24-811 and 1600-1622 contain a biallelic marker

or single nucleotide polymorphism (SNP) with respect to a reference nucleotide sequence. This single nucleotide polymorphism may comprise a single base substitution, insertion, or deletion, while this biallelic marker may comprise abour one to ten consecutive bases substituted, inserted or deleted.

Another aspect of the present invention is a method for determining the level of homology 5 between a polypeptide code of SEQ ID NOS. 812-1599 and a reference polypeptide sequence, comprising the steps of reading the polypeptide code of SEQ ID NOS. 812-1599 and the reference polypeptide sequence through use of a computer program which determines homology levels and determining homology between the polypeptide code and the reference polypeptide sequence using the computer program.

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Accordingly, another aspect of the present invention is a method for determining whether a nucleic acid code of SEQ ID NOs. 24-811 and 1600-1622 differs at one or more nucleotides from a reference nucleotide sequence comprising the steps of reading the nucleic acid code and the reference nucleotide sequence through use of a computer program which identifies differences between nucleic acid sequences and identifying differences between the nucleic acid code and the reference nucleotide 15 sequence with the computer program. In some embodiments, the computer program is a program which identifies single nucleotide polymorphisms. The method may be implemented by the computer systems described above and the method illustrated in Figure 8. The method may also be performed by reading at least 2, 5, 10, 15, 20, 25, 30, or 50 of the nucleic acid codes of SEQ ID NOs. 24-811 and 1600-1622 and the reference nucleotide sequences through the use of the computer program and identifying differences 20 between the nucleic acid codes and the reference nucleotide sequences with the computer program.

In other embodiments the computer based system may further comprise an identifier for identifying features within the nucleotide sequences of the nucleic acid codes of SEQ ID NOs. 24-811 and 1600-1622 or the amino acid sequences of the polypeptide codes of SEQ ID NOS. 812-1599.

An "identifier" refers to one or more programs which identifies certain features within the 25 above-described nucleotide sequences of the nucleic acid codes of SEQ ID NOs. 24-811 and 1600-1622 or the amino acid sequences of the polypeptide codes of SEQ ID NOS. 812-1599. In one embodiment, the identifier may comprise a program which identifies an open reading frame in the cDNAs codes of SEQ ID NOs. 24-811 and 1600-1622.

Figure 9 is a flow diagram illustrating one embodiment of an identifier process 300 for 30 detecting the presence of a feature in a sequence. The process 300 begins at a start state 302 and then moves to a state 304 wherein a first sequence that is to be checked for features is stored to a memory 115 in the computer system 100. The process 300 then moves to a state 306 wherein a database of sequence features is opened. Such a database would include a list of each feature's attributes along with the name of the feature. For example, a feature name could be "Initiation Codon" and the 35 attribute would be "ATG". Another example would be the feature name "TAATAA Box" and the feature attribute would be "TAATAA". An example of such a database is produced by the University of Wisconsin Genetics Computer Group (www.gcg.com).

Once the database of features is opened at the state 306, the process 300 moves to a state 308 wherein the first feature is read from the database. A comparison of the attribute of the first feature with the first sequence is then made at a state 310. A determination is then made at a decision state 316 whether the attribute of the feature was found in the first sequence. If the attribute was found, 5 then the process 300 moves to a state 318 wherein the name of the found feature is displayed to the user.

The process 300 then moves to a decision state 320 wherein a determination is made whether move features exist in the database. If no more features do exist, then the process 300 terminates at an end state 324. However, if more features do exist in the database, then the process 300 reads the 10 next sequence feature at a state 326 and loops back to the state 310 wherein the attribute of the next feature is compared against the first sequence.

It should be noted, that if the feature attribute is not found in the first sequence at the decision state 316, the process 300 moves directly to the decision state 320 in order to determine if any more features exist in the database.

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In another embodiment, the identifier may comprise a molecular modeling program which determines the 3-dimensional structure of the polypeptides codes of SEQ ID NOS. 812-1599. In some embodiments, the molecular modeling program identifies target sequences that are most compatible with profiles representing the structural environments of the residues in known threedimensional protein structures. (See, e.g., Eisenberg et al., U.S. Patent No. 5,436,850 issued July 25, 20 1995). In another technique, the known three-dimensional structures of proteins in a given family are superimposed to define the structurally conserved regions in that family. This protein modeling technique also uses the known three-dimensional structure of a homologous protein to approximate the structure of the polypeptide codes of SEQ ID NOS. 812-1599. (See e.g., Srinivasan, et al., U.S. Patent No. 5,557,535 issued September 17, 1996). Conventional homology modeling techniques 25 have been used routinely to build models of proteases and antibodies. (Sowdhamini et al., Protein Engineering 10:207, 215 (1997)). Comparative approaches can also be used to develop threedimensional protein models when the protein of interest has poor sequence identity to template proteins. In some cases, proteins fold into similar three-dimensional structures despite having very weak sequence identities. For example, the three-dimensional structures of a number of helical 30 cytokines fold in similar three-dimensional topology in spite of weak sequence homology.

The recent development of threading methods now enables the identification of likely folding patterns in a number of situations where the structural relatedness between target and template(s) is not detectable at the sequence level. Hybrid methods, in which fold recognition is performed using Multiple Sequence Threading (MST), structural equivalencies are deduced from the threading output 35 using a distance geometry program DRAGON to construct a low resolution model, and a full-atom representation is constructed using a molecular modeling package such as QUANTA.

According to this 3-step approach, candidate templates are first identified by using the novel fold recognition algorithm MST, which is capable of performing simultaneous threading of multiple aligned sequences onto one or more 3-D structures. In a second step, the structural equivalencies obtained from the MST output are converted into interresidue distance restraints and fed into the distance geometry program DRAGON, together with auxiliary information obtained from secondary structure predictions. The program combines the restraints in an unbiased manner and rapidly generates a large number of low resolution model confirmations. In a third step, these low resolution model confirmations are converted into full-atom models and subjected to energy minimization using the molecular modeling package QUANTA. (See e.g., Aszódi et al., Proteins:Structure, Function, and Genetics, Supplement 1:38-42 (1997)).

The results of the molecular modeling analysis may then be used in rational drug design techniques to identify agents which modulate the activity of the polypeptide codes of SEQ ID NOS. 812-1599.

Accordingly, another aspect of the present invention is a method of identifying a feature

within the nucleic acid codes of SEQ ID NOs. 24-811 and 1600-1622 or the polypeptide codes of

SEQ ID NOS. 812-1599 comprising reading the nucleic acid code(s) or the polypeptide code(s)

through the use of a computer program which identifies features therein and identifying features

within the nucleic acid code(s) or polypeptide code(s) with the computer program. In one

embodiment, computer program comprises a computer program which identifies open reading

frames. In a further embodiment, the computer program identifies structural motifs in a polypeptide

sequence. In another embodiment, the computer program comprises a molecular modeling program.

The method may be performed by reading a single sequence or at least 2, 5, 10, 15, 20, 25, 30, or 50 of
the nucleic acid codes of SEQ ID NOs. 24-811 and 1600-1622 or the polypeptide codes of SEQ ID

NOS. 812-1599 through the use of the computer program and identifying features within the nucleic

acid codes or polypeptide codes with the computer program.

The nucleic acid codes of SEQ ID NOs. 24-811 and 1600-1622 or the polypeptide codes of SEQ ID NOS. 812-1599 may be stored and manipulated in a variety of data processor programs in a variety of formats. For example, the nucleic acid codes of SEQ ID NOs. 24-811 and 1600-1622 or the polypeptide codes of SEQ ID NOS. 812-1599 may be stored as text in a word processing file, such as MicrosoftWORD or WORDPERFECT or as an ASCII file in a variety of database programs familiar to those of skill in the art, such as DB2, SYBASE, or ORACLE. In addition, many computer programs and databases may be used as sequence comparers, identifiers, or sources of reference nucleotide or polypeptide sequences to be compared to the nucleic acid codes of SEQ ID NOs. 24-811 and 1600-1622 or the polypeptide codes of SEQ ID NOS. 812-1599. The following list is intended not to limit the invention but to provide guidance to programs and databases which are useful with the nucleic acid codes of SEQ ID NOS. 24-811 and 1600-1622 or the polypeptide codes of SEQ ID NOS. 812-1599. The programs and databases which may be used include, but are not limited to: MacPattern (EMBL),

147 DiscoveryBase (Molecular Applications Group), GeneMine (Molecular Applications Group), Look (Molecular Applications Group), MacLook (Molecular Applications Group), BLAST and BLAST2 (NCBI), BLASTN and BLASTX (Altschul et al, J. Mol. Biol. 215: 403 (1990)), FASTA (Pearson and Lipman, Proc. Natl. Acad. Sci. USA, 85: 2444 (1988)), FASTDB (Brutlag et al. Comp. App. Biosci. 5 6:237-245, 1990), Catalyst (Molecular Simulations Inc.), Catalyst/SHAPE (Molecular Simulations Inc.), Cerius².DBAccess (Molecular Simulations Inc.), HypoGen (Molecular Simulations Inc.), Insight II, (Molecular Simulations Inc.), Discover (Molecular Simulations Inc.), CHARMm (Molecular Simulations Inc.), Felix (Molecular Simulations Inc.), DelPhi, (Molecular Simulations Inc.), QuanteMM, (Molecular Simulations Inc.), Homology (Molecular Simulations Inc.), Modeler (Molecular Simulations 10 Inc.), ISIS (Molecular Simulations Inc.), Quanta/Protein Design (Molecular Simulations Inc.), WebLab (Molecular Simulations Inc.), WebLab Diversity Explorer (Molecular Simulations Inc.), Gene Explorer (Molecular Simulations Inc.), SeqFold (Molecular Simulations Inc.), the EMBL/Swissprotein database, the MDL Available Chemicals Directory database, the MDL Drug Data Report data base, the Comprehensive Medicinal Chemistry database, Derwents's World Drug Index database, the 15 BioByteMasterFile database, the Genbank database, and the Genseqn database. Many other programs

Motifs which may be detected using the above programs include sequences encoding leucine zippers, helix-turn-helix motifs, glycosylation sites, ubiquitination sites, alpha helices, and beta sheets, signal sequences encoding signal peptides which direct the secretion of the encoded proteins, 20 sequences implicated in transcription regulation such as homeoboxes, acidic stretches, enzymatic active sites, substrate binding sites, and enzymatic cleavage sites.

and data bases would be apparent to one of skill in the art given the present disclosure.

EXAMPLE 62

Methods of Making Nucleic Acids

25 The present invention also comprises methods of making the EST-related nucleic acids, fragments of EST-related nucleic acids, positional segments of the EST-related nucleic acids, or fragments of positional segments of the EST-related nucleic acids. The methods comprise sequentially linking together nucleotides to produce the nucleic acids having the preceding sequences. A variety of methods of synthesizing nucleic acids are known to those skilled in the art.

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In many of these methods, synthesis is conducted on a solid support. These included the 3' phosphoramidite methods in which the 3' terminal base of the desired oligonucleotide is immobilized on an insoluble carrier. The nucleotide base to be added is blocked at the 5' hydroxyl and activated at the 3' hydroxyl so as to cause coupling with the immobilized nucleotide base. Deblocking of the new immobilized nucleotide compound and repetition of the cycle will produce the desired 35 polynucleotide. Alternatively, polynucleotides may be prepared as described in U.S. Patent No. 5,049,656. In some embodiments, several polynucleotides prepared as described above are ligated together to generate longer polynucleotides having a desired sequence.

EXAMPLE 63

Methods of Making Polypeptides

The present invention also comprises methods of making the polynucleotides encoded by ESTrelated nucleic acids, fragments of EST-related nucleic acids, positional segments of the EST-related nucleic acids and methods of making the EST-related polypeptides, fragments of EST-related polypeptides, positional segments of EST-related polypeptides, or fragments of EST-related polypeptides. The methods comprise sequentially linking together amino acids to produce the nucleic polypeptides having the preceding sequences. In some embodiments, the polypeptides made by these methods are 150 amino acids or less in length. In other embodiments, the polypeptides made by these methods are 120 amino acids or less in length.

A variety of methods of making polypeptides are known to those skilled in the art, including methods in which the carboxyl terminal amino acid is bound to polyvinyl benzene or another suitable resin. The amino acid to be added possesses blocking groups on its amino moiety and any side chain reactive groups so that only its carboxyl moiety can react. The carboxyl group is activated with carbodiimide or another activating agent and allowed to couple to the immobilized amino acid. After removal of the blocking group, the cycle is repeated to generate a polypeptide having the desired sequence. Alternatively, the methods described in U.S. Patent No. 5,049,656 may be used.

20 As discussed above, the EST-related nucleic acids, fragments of the EST-related nucleic acids, positional segments of the EST-related nucleic acids, or fragments of positional segments of the EST-related nucleic acids can be used for various purposes. The polynucleotides can be used to express recombinant protein for analysis, characterization or therapeutic use; production of secreted polypeptides or chimeric polypeptides, antibody production, as markers for tissues in which the 25 corresponding protein is preferentially expressed (either constitutively or at a particular stage of tissue differentiation or development or in disease states); as molecular weight markers on Southern gels; as chromosome markers or tags (when labeled) to identify chromosomes or to map related gene positions; to compare with endogenous DNA sequences in patients to identify potential genetic disorders; as probes to hybridize and thus discover novel, related DNA sequences; as a source of information to derive PCR 30 primers for genetic fingerprinting; for selecting and making oligomers for attachment to a "gene chip" or other support, including for examination for expression patterns; to raise anti-protein antibodies using DNA immunization techniques; and as an antigen to raise anti-DNA antibodies or elicit another immune response. Where the polynucleotide encodes a protein or polypeptide which binds or potentially binds to another protein or polypeptide (such as, for example, in a receptor-ligand interaction), the polynucleotide 35 can also be used in interaction trap assays (such as, for example, that described in Gyuris et al., Cell 75:791-803 (1993)) to identify polynucleotides encoding the other protein or polypeptide with which binding occurs or to identify inhibitors of the binding interaction.

The proteins or polypeptides provided by the present invention can similarly be used in assays to determine biological activity, including in a panel of multiple proteins for high-throughput screening; to raise antibodies or to elicit another immune response; as a reagent (including the labeled reagent) in assays designed to quantitatively determine levels of the protein (or its receptor) in biological fluids; as markers for tissues in which the corresponding protein is preferentially expressed (either constitutively or at a particular stage of tissue differentiation or development or in a disease state); and, of course, to isolate correlative receptors or ligands. Where the protein or polypeptide binds or potentially binds to another protein or polypeptide (such as, for example, in a receptor-ligand interaction), the protein can be used to identify the other protein with which binding occurs or to identify inhibitors of the binding interaction. Proteins or polypeptides involved in these binding interactions can also be used to screen for peptide or small molecule inhibitors or agonists of the binding interaction.

Any or all of these research utilities are capable of being developed into reagent grade or kit format for commercialization as research products.

Methods for performing the uses listed above are well known to those skilled in the art.

References disclosing such methods include without limitation "Molecular Cloning; A Laboratory Manual," 2d ed., Cold Spring Harbor Laboratory Press, Sambrook, J., E.F. Fritsch and T. Maniatis eds., 1989, and "Methods in Enzymology; Guide to Molecular Cloning Techniques," Academic Press, Berger, S.L. and A.R. Kimmel eds., 1987.

Polynucleotides and proteins or polypeptides of the present invention can also be used as
nutritional sources or supplements. Such uses include without limitation use as a protein or amino acid
supplement, use as a carbon source, use as a nitrogen source and use as a source of carbohydrate. In
such cases the protein or polynucleotide of the invention can be added to the feed of a particular
organism or can be administered as a separate solid or liquid preparation, such as in the form of powder,
pills, solutions, suspensions or capsules. In the case of microorganisms, the protein or polynucleotide of
the invention can be added to the medium in or on which the microorganism is cultured.

Although this invention has been described in terms of certain preferred embodiments, other embodiments which will be apparent to those of ordinary skill in the art in view of the disclosure herein are also within the scope of this invention. Accordingly, the scope of the invention is intended to be limited only by reference to the appended claims.

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Sequence Listing Free Text

The following free text appears in the accompanying Sequence Listing:

Von Heijne matrix

score

35 sequence

name

martinspector prediction

150 CLAIMS

- A purified nucleic acid comprising a sequence selected from the group consisting of SEQ ID NOs. 24-811 and SEQ ID NOs. 1600-1622 and sequences complementary to the sequences of SEQ ID NOs. 24-811 and SEQ ID NOs. 1600-1622.
 - A purified nucleic acid comprising at least 15 consecutive nucleotides of a sequence selected from the group consisting of SEQ ID NOs. 24-811 and SEQ ID NOs. 1600-1622 and sequences complementary to the sequences of SEQ ID NOs. 24-811 and SEQ ID NOs. 1600-1622.
 - 3. A purified or isolated polypeptide comprising a sequence selected from the group consisting of the sequences of SEQ ID NOs. 812-1599.
 - 4. A method of making a cDNA comprising the steps of:
- a) contacting a collection of mRNA molecules from human cells with a primer comprising at least 15 consecutive nucleotides of a sequence selected from the group consisting of the sequences complementary to SEQ ID NOs. 24-811 and SEQ ID NOs. 1600-1622;
 - b) hybridizing said primer to an mRNA in said collection that encodes said protein;
- c) reverse transcribing said hybridized primer to make a first cDNA strand from said mRNA;
 - d) making a second cDNA strand complementary to said first cDNA strand; and
 - e) isolating the resulting cDNA comprising said first cDNA strand and said second cDNA strand.
- 25 5. A method of making a cDNA comprising the steps of:
 - a) obtaining a cDNA comprising a sequence selected from the group consisting of SEQ ID NOs. 24-811 and SEQ ID NOs. 1600-1622;
- b) contacting said cDNA with a detectable probe comprising at least 15 consecutive nucleotides of a sequence selected from the group consisting of SEQ ID NOs. 24-811 and SEQ ID
 NOs. 1600-1622 and the sequences complementary to SEQ ID NOs. 24-811 and SEQ ID NOs. 1600-1622 under conditions which permit said probe to hybridize to said cDNA;
 - c) identifying a cDNA which hybridizes to said detectable probe; and
 - d) isolating said cDNA which hybridizes to said probe.
- 35 6. A method of making a cDNA comprising the steps of:
 - a) contacting a collection of mRNA molecules from human cells with a first primer capable of hybridizing to the polyA tail of said mRNA;
 - b) hybridizing said first primer to said polyA tail;

- c) reverse transcribing said mRNA to make a first cDNA strand;
- d) making a second cDNA strand complementary to said first cDNA strand using at least one primer comprising at least 15 consecutive nucleotides of a sequence selected from the group consisting of SEQ ID NOs. 24-811 and SEQ ID NOs. 1600-1622; and
- e) isolating the resulting cDNA comprising said first cDNA strand and said second cDNA strand.
 - 7. A method of making a polypeptide comprising the steps of:
- a) obtaining a cDNA which encodes a polypeptide encoded by a nucleic acid comprising
 10 a sequence selected from the group consisting of SEQ ID NOs. 24-811 or a cDNA which encodes a polypeptide comprising at least 10 consecutive amino acids of a polypeptide encoded by a sequence selected from the group consisting of SEQ ID NOs. 24-811;
 - b) inserting said cDNA in an expression vector such that said cDNA is operably linked to a promoter;
 - c) introducing said expression vector into a host cell whereby said host cell produces the protein encoded by said cDNA; and
 - d) isolating said protein.

- 8. In an array of discrete ESTs or fragments thereof of at least 15 nucleotides in length, the improvement comprising inclusion in said array of at least one sequence selected from the group consisting of SEQ ID NOs. 24-811 and SEQ ID NOs. 1600-1622, the sequences complementary to the sequences of SEQ ID NOs. 24-811 and SEQ ID NOs. 1600-1622 and fragments comprising at least 15 consecutive nucleotides of said sequence.
- 9. The array of Claim 8 including therein at least five sequences selected from the group consisting of SEQ ID NOs. 24-811 and SEQ ID NOs. 1600-1622, the sequences complementary to the sequences of SEQ ID NOs. 24-811 and SEQ ID NOs. 1600-1622 and fragments comprising at least 15 consecutive nucleotides of said sequences.
- 30 10. An enriched population of recombinant nucleic acids, said recombinant nucleic acids comprising an insert nucleic acid and a backbone nucleic acid, wherein at least 5% of said insert nucleic acids in said population comprise a sequence selected from the group consisting of SEQ ID NOs. 24-811 and SEQ ID NOs. 1600-1622, the sequences complementary to SEQ ID NOs. 24-811 and SEQ ID NOs. 1600-1622 and fragments comprising at least 15 consecutive nucleotides of said sequences.
 - 11. An antibody composition capable of selectively binding to an epitope-containing fragment of a polypeptide comprising a contiguous span of at least 8 amino acids of any of SEQ ID NOs. 812-1599, wherein said antibody is polyclonal or monoclonal.

- 12. A computer readable medium having stored thereon a sequence selected from the group consisting of a nucleic acid code of SEQ ID NOs. 24-811 and 1600-1622 and a polypeptide code of SEQ ID NOs. 812-1599.
- 13. A computer system comprising a processor and a data storage device wherein said data storage device has stored thereon a sequence selected from the group consisting of a nucleic acid code of SEOID NOs. 24-811 and 1600-1622 and a polypeptide code of SEQ ID NOs. 812-1599.
- 10 14. The computer system of Claim 13 further comprising a sequence comparer and a data storage device having reference sequences stored thereon.
 - 15. The computer system of Claim 14 wherein said sequence comparer comprises a computer program which indicates polymorphisms.
 - 16. The computer system of Claim 13 further comprising an identifier which identifies features in said sequence.
- 17. A method for comparing a first sequence to a reference sequence wherein said first sequence is selected from the group consisting of a nucleic acid code of SEQID NOs. 24-811 and 1600-1622 and a polypeptide code of SEQ ID NOs. 812-1599 comprising the steps of:
 - a) reading said first sequence and said reference sequence through use of a computer program which compares sequences; and
- b) determining differences between said first sequence and said reference sequence with said computer program.
 - 18. The method of Claim 17, wherein said step of determining differences between the first sequence and the reference sequence comprises identifying polymorphisms.
- 30 19. A method for identifying a feature in a sequence selected from the group consisting of a nucleic acid code of SEQID NOs. 24-811 and 1600-1622 and a polypeptide code of SEQ ID NOs. 812-1599 comprising the steps of:
 - a) reading said sequence through the use of a computer program which identifies features in sequences; and
- b) identifying features in said sequence with said computer program.
 - 20. A vector comprising a nucleic acid according to either Claims 1 or 2.
 - 21. A host cell containing a nucleic acid of Claim 20.

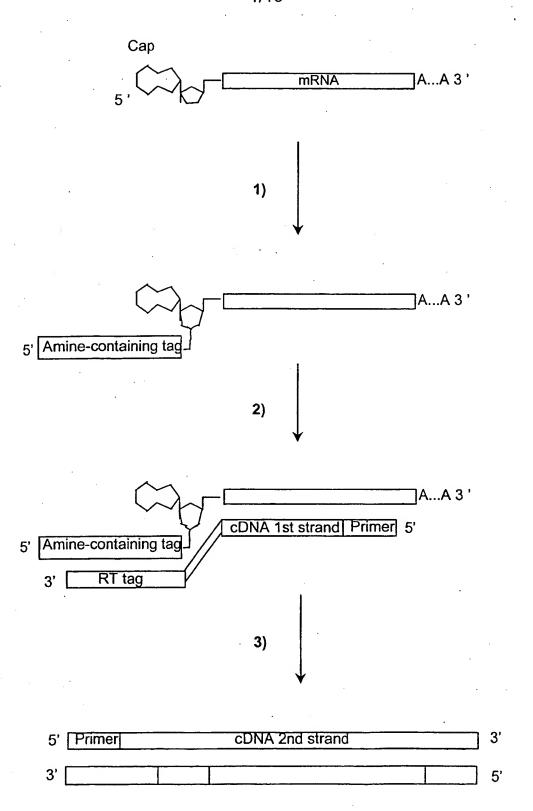


Figure 1

Minimum signal peptide score	false positive rate	false negative rate	proba(0.1)	proba(0.2)
3,5	0,121	0,036	0,467	0,664
4	0,096	0,06	0,519	0,708
4,5	0,078	0,079	0,565	0,745
5	0,062	0,098	0,615	0,782
5,5	0,05	0,127	0,659	0,813
6	0,04	0,163	0,694	0,836
6,5	0,033	0,202	0,725	0,855
7	0,025	0,248	0,763	0,878
7,5	0,021	0,304	0,78	0,889
8	0,015	0,368	0,816	0,909
8,5	0,012	0,418	0,836	0,92
9	0,009	0,512	0,856	0,93
9,5	0,007	0,581	0,863	0,934
10	0,006	0,679	0,835	0,919

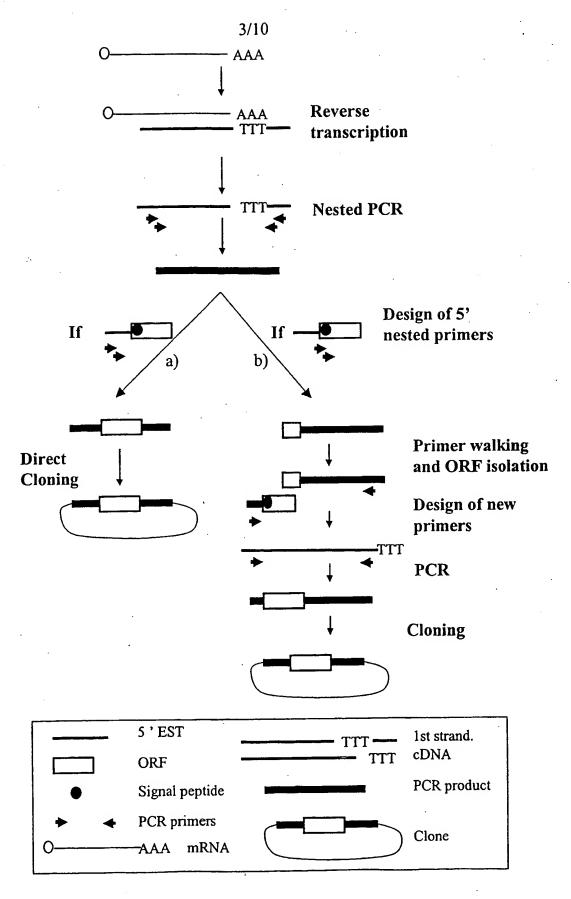


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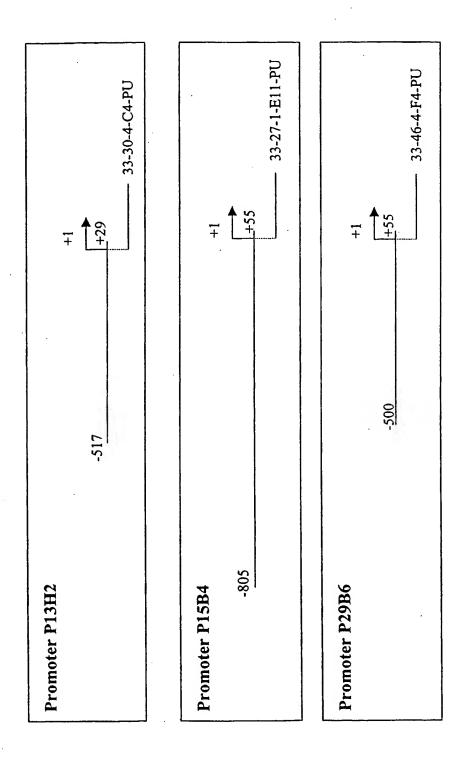


Figure 4

5/10

Promoter sequence P13H2 (546 bp):

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CMYB_01	-502	+	0.983	9	TGTCAGTTG
MYOD_Q6	-501	-	0.961	10	CCCAACTGAC
S8_01	-444	-	0.960	· 11	AATAGAATTAG
S8_01	-425	+	0.966	11	AACTAAATTAG
DELTAEF1_01	-390	-	0.960	11	GCACACCTCAG
GATA_C	-364	-	0.964	11	AGATAAATCCA
CMYB_01	-349	+	0.958	9	CTTCAGTTG
GATA1_02	-343	+	0.959	14	TTGTAGATAGGACA
GATA_C	-339	+	0.953	11	AGATAGGACAT
TAL1ALPHAE47_01	-235	+	0.973	16	CATAACAGATGGTAAG
TAL1BETAE47_01	-235	+	0.983	16	CATAACAGATGGTAAG
TAL1BETAITF2_01	-235	+	0.978	16	CATAACAGATGGTAAG
MYOD_Q6	-232	-	0.954	10	ACCATCTGTT
GATA1_04	-217	-	0.953	13	TCAAGATAAAGTA
IK1_01	-126	+	0.963	13	AGTTGGGAATTCC
IK2_01	-126	+	0.985	12	AGTTGGGAATTC
CREL_01	-123	+	0.962	10	TGGGAATTCC
GATA1_02	-9 6	+	0.950	14	TCAGTGATATGGCA
SRY_02	-41	-	0.951	12	TAAAACAAAACA
E2F_02	-33	+	0.957	8	TTTAGCGC
MZF1_01	-5	-	0.975	8	TGAGGGGA

Promoter sequence P15B4 (861bp):

		Orient			
Matrix	Position	ation	Score	Length	Sequence
NFY_Q6	-748	-	0.956	11	GGACCAATCAT
MZF1_01	-738	+	0.962	8	CCTGGGGA
CMYB_01	-684	+	0.994	9	TGACCGTTG
VMYB_02	-682	-	0.985	9	TCCAACGGT
STAT_01	-673	+	0.968	9	TTCCTGGAA
STAT_01	-673	-	0.951	9	TTCCAGGAA
MZF1_01	-556	-	0.956	8	TTGGGGGA
IK2_01	-451	+	0.965	12	GAATGGGATTTC
MZF1_01	-424	+	0.986	8	AGAGGGGA
SRY_02	-398	-	0.955	12	GAAAACAAAACA
MZF1_01	-216		0.960	8	GAAGGGGA
MYOD_Q6	-190	+	0.981	10	AGCATCTGCC
DELTAEF1_01	-176		0.958	11	TCCCACCTTCC
S8_01	5		0.992	11	GAGGCAATTAT
MZF1_01	16		0.986	8	AGAGGGGA

Promoter sequence P29B6 (555 bp):

Orient

Matrix	Position	ation	Score	Length	Sequence
ARNT_01	-311	+	0.964	16	GGACTCACGTGCTGCT
NMYC_01	-309	+	0.965	12	ACTCACGTGCTG
USF_01	-309	+	0.985	12	ACTCACGTGCTG
USF_01	-309	-	0.985	12	CAGCACGTGAGT
NMYC_01	-309		0.956	12	CAGCACGTGAGT
MYCMAX_02	-309		0.972	12	CAGCACGTGAGT
USF_C	-307	+	0.997	8	TCACGTGC
USF_C	-307	-	0.991	8	GCACGTGA
MZF1_01	-292		0.968	8	CATGGGGA
ELK1_02	-105		0.963	14	CTCTCCGGAAGCCT
CETS1P54_01	-102	+	0.974	10	TCCGGAAGCC
AP1_Q4	-42	-	0.963	11	AGTGACTGAAC
AP1FJ_Q2	-42	-	0.961	11	AGTGACTGAAC
PADS_C	45	+	1.000	9	TGTGGTCTC

Figure 5

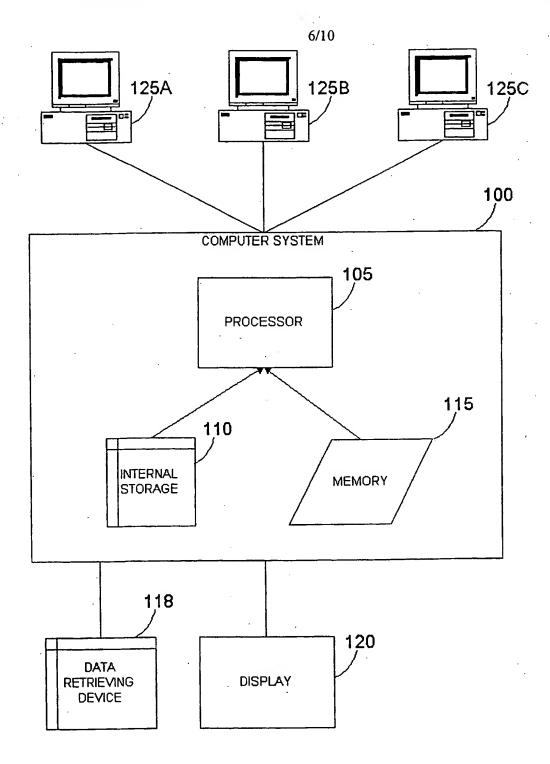


FIGURE 6

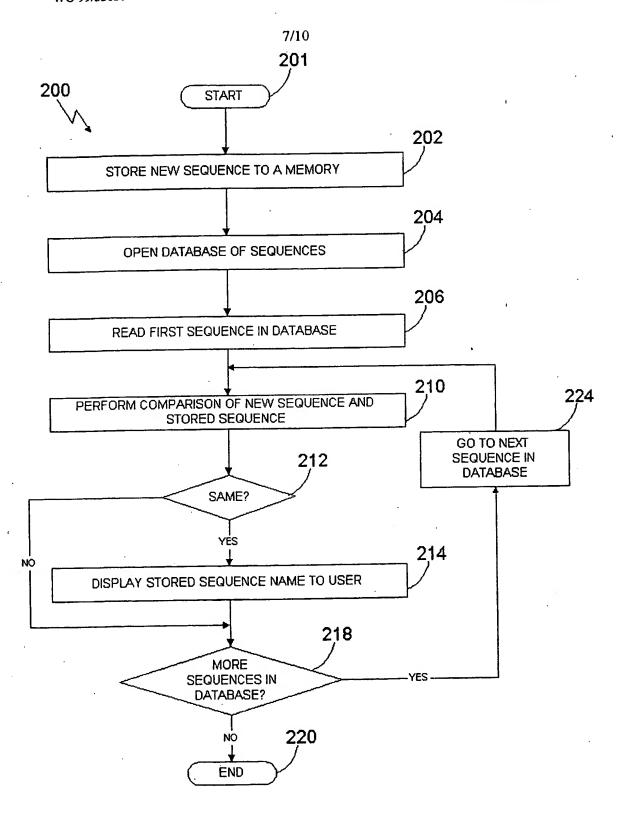
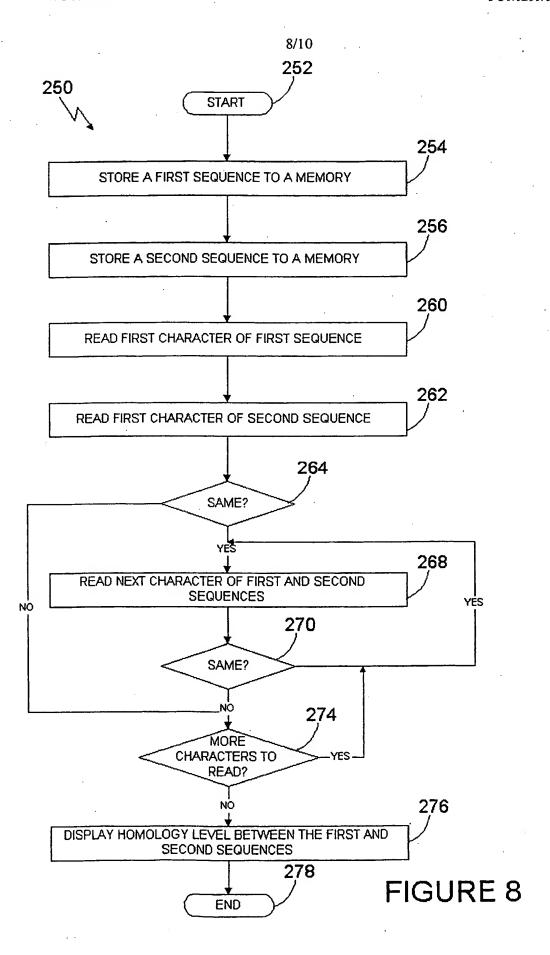
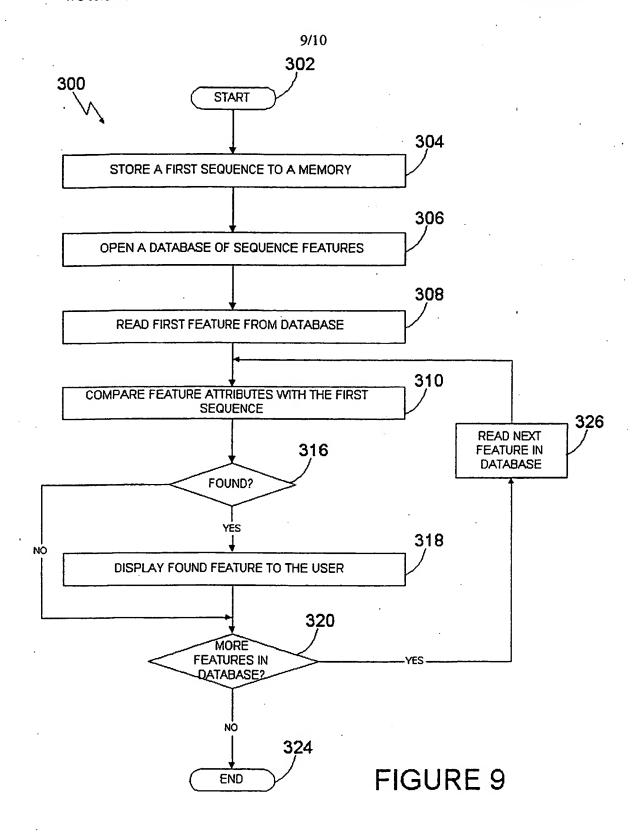


FIGURE 7





	Search characteristic	stic			Selection	Selection Characteristics
Step	Program	Strand	Parameters	Identity (%)	Identity (%) Length (bp)	Comments
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tRNA	FASTA	both	•	80	09	
rRNA	BLASTN	both	S=108	08	40	
mtRNA	BLASTN	both	S=108	80	40	
Procaryotic	BLASTN	both	S=144	06	40	
Fungal	BLASTN	both	S=144	90	40	
Alu	BEASTN	both	S=72, B=5	70	40	max 5 matches, masking
L1	BLASTN	both	S=72, B=5	70	40	max 5 matches, masking
Repeats	BLASTN	both	S=72	70	40	masking
			W=6, S=10, E=1000,			
PolyA	BLAST2N	top	N=12	90	10	in the last 100 nucleotides
Polyadenylation signal	•	top	AATAAA allowing 1 mismatch	owing 1 misn	natch	in the 50 nucleotides before the 5' end of the polA
Vertebrate	BLASTN then FASTA	both	•	90 then 70	30	first BLASTN, then FASTA on maching sequences
ESTs	BLAST2N	both	4	90	30	
Genesed	BLASTN	both	W=8, B=10	90	30	
ORF	BLASTP	top	W=8, B=10		•	on ORF proteins, max 10 matches
Proteins	BLASTX	top	E = 0.001	70	30	

Figure 10

SEQUENCE LISTING

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caa	gca		agg	aga	caa	aaa	cag	gag	acc	tica	aac	cct	ccc	cgt	acc	24	15
														Arg		-	• •
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מי בכ	-~39 <u>'</u>	,	-3341		- J - C		-949(		-ugc'	ccca	229	- 333	,,,,, ,	3	u	47.	•

1602

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18

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                                                                     300
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catteetgte tgcattagta acteecaace tagatgtgaa aacttagtte ttteteatag
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Val Gln Trp Arg Asp Leu Cys Ser Leu Gln Pro Gln Leu Pro Arg Phe 10 15 20	
ggg cca tcc tcc tgc ctc agc ctc cca agt ggc tgg gac tgc agg cgc	195
Gly Pro Ser Ser Cys Leu Ser Leu Pro Ser Gly Trp Asp Cys Arg Arg 25 30 35	
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Ser Pro	231
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Leu Leu Leu Leu Gly Ala Trp Ala Ile Pro Gly Gly Leu Gly Asp	
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Arg Ala Pro Leu Thr Ala Thr Ala Pro Gln Leu Asp Asp Glu Glu Met 10 20	
tac tca gcc cac atg ccc gct cac ctg cgc tgt gat gcc tgc aga gct	199
Tyr Ser Ala His Met Pro Ala His Leu Arg Cys Asp Ala Cys Arg Ala 25 30 35	
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	ctg Leu															100
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	cag Gln			gag					gct					gga		151

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Leu Pro Pro Pro Gly Ser Cys Ala Gly Arg Arg Ser Pro Xaa Thr Pro

-5 qac qag tot acc cca cct ccc cgg aag aag aag gat att cgc gat 195 Asp Glu Ser Thr Pro Pro Pro Arg Lys Lys Lys Asp Ile Arg Asp 10 tac aat gat gca gac atg gcg cgt ctt ctg gag caa ggg gag ggg 240 Tyr Asn Asp Ala Asp Met Ala Arg Leu Leu Glu Gln Gly Glu Gly 30 35

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-15

256

448

461

qct ctt tta gaa ggt gtc caa tgt gac gtg gaa tta gtg gag tct ggg 160 Ala Leu Leu Glu Gly Val Gln Cys Asp Val Glu Leu Val Glu Ser Gly

208 ggc ggc ttg gtg cag cct gga ggg tct ctg aga ctt tcc tgt gca gcc Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala 15

tot gga tto aat ttt ago act tat gag atg cat tgg atc cgc cag gct

Ser Gly Phe Asn Phe Ser Thr Tyr Glu Met His Trp Ile Arg Gln Ala 30 35

cca qqq aag ggg ccg gag tgg gtn nca tat gtc agt ggt gga ggt gga 304 Pro Gly Lys Gly Pro Glu Trp Val Xaa Tyr Val Ser Gly Gly Gly Gly

50 acc agh nnn aac gev sac tet gtg aag gge ega tte acc ate tee aga 352 Thr Xaa Xaa Asn Ala Xaa Ser Val Lys Gly Arg Phe Thr Ile Ser Arg

65 gac aat gcc aac agt ttt gtg tat cta caa atg gac agt ctg cga gtc 400 Asp Asn Ala Asn Ser Phe Val Tyr Leu Gln Met Asp Ser Leu Arg Val

gag gac acc gct ctc tat tac tgt gcg aga rgg gat tac gac ttc tgg Glu Asp Thr Ala Leu Tyr Tyr Cys Ala Arg Xaa Asp Tyr Asp Phe Trp

90 95 agt ggt tat tat a

Ser Gly Tyr Tyr

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                                                                   174
                                Met Asp Val Gly Pro Ser Ser Leu
                                            -25
ccc cac ctt ggg ctg aag ctg ctg ctg ctc ctg ctg ctg ccc ctc
                                                                   222
Pro His Leu Gly Leu Lys Leu Leu Leu Leu Leu Leu Leu Leu Pro Leu
                                       -10
agg ggc caa gcc aac aca ggc tgc tac ggg atc cca ggg atg ccc ggc
                                                                   270
Arg Gly Gln Ala Asn Thr Gly Cys Tyr Gly Ile Pro Gly Met Pro Gly
ctg ccc ggg gca cca ggg aag gat ggg tac gac gga ctg ccg ggg ccc
                                                                   318
Leu Pro Gly Ala Pro Gly Lys Asp Gly Tyr Asp Gly Leu Pro Gly Pro
aag ggg gag cca gga atc cca gcc att ccc ggg atc cga gga ccc aaa
                                                                   366
Lys Gly Glu Pro Gly Ile Pro Ala Ile Pro Gly Ile Arg Gly Pro Lys
   30
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Gly Gln Lys Gly Glu Pro Gly Leu Pro Gly His Pro Gly Lys Asn Gly
ccc atg gga ccc cct ggg atg cca
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Pro Met Gly Pro Pro Gly Met Pro
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ctg t Leu P	he L												gct	gtg			103
act of Thr G													_				151
acc t Thr C																	199
tgg t		3ln (247
acg t Thr F	Phe A																295
ctg g	gg 9	gc a	aaa	gct	gtc	ctg	act	ctt	tcg	gat	gcg	caa	cct	gac	gat		343

Leu Gly Gly Lys Ala Val Leu Thr Leu Ser Asp Ala Gln Pro Asp Asp 75 gag gct gaa tat tat tgt gtc ctc tcc tat agt ggt ggt cgg ccg gtg 391 Glu Ala Glu Tyr Tyr Cys Val Leu Ser Tyr Ser Gly Gly Arg Pro Val 90 100 ttc ggc gga ggg acc aag ctg acc gtc cta agt cag 427 Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Ser Gln <210> 40 <211> 97 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 22..96 <221> sig_peptide <222> 22..84 <223> Von Heijne matrix score 11.8999996185303 seq LALCLLLGPLAGA/KP agatcaggaa gcaccgggaa g atg cag gcc tgc atg gtg ccg ggg ctg gcc 51 Met Gln Ala Cys Met Val Pro Gly Leu Ala -20 ctc tgc ctc cta ctg ggg cct ctt gca ggg gcc aag cct gtg cag g Leu Cys Leu Leu Gly Pro Leu Ala Gly Ala Lys Pro Val Gln -10 - 5 <210> 41 <211> 536 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 266..535 <221> sig_peptide <222> 266..307 <223> Von Heijne matrix score 15 seq LLPLLLLLPMCWA/VE <400> 41 actittgggg tcacgtgctc attccgtttc cctacctccc ccaaccttat cccgccctg 60 ggggttcgcg ggcatttttc aggaactttc tttccggctt gagaagccgc cactcccaag 120 atgsagcagg aaccgcggct gctggacaag aggggtgcgg tggatactga cctttgctcc 180 ggcctcgtcg tgaagacaca gcgcatctcc ccgctgtagg cttcctccca cagaacccgt 240 ttcgggcctc agagcgtctg gtgag atg ctg ttg ccg ctg ctg ctg cta 292 Met Leu Leu Pro Leu Leu Leu Leu -10 ccc atg tgc tgg gcc gtg gag gtc aag agg ccc cgg ggc gtc tcc ctc 340 Pro Met Cys Trp Ala Val Glu Val Lys Arg Pro Arg Gly Val Ser Leu 1 5 acc aat cat cac tto tac gat gag too aag cot tto acc tgo otg gac 388 Thr Asn His His Phe Tyr Asp Glu Ser Lys Pro Phe Thr Cys Leu Asp 15 20 ggt tcg gcc acc atc cca ttt gat cag gtc aac gat gac tat tgc gac 436

Gly Ser Ala Thr Ile Pro Phe Asp Gln Val Asn Asp Asp Tyr Cys Asp

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35
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                                                                       484
Cys Lys Asp Gly Ser Asp Glu Pro Gly Thr Ala Ala Cys Pro Asn Gly
                         50
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Ser Phe His Cys Thr Asn Thr Gly Tyr Lys Pro Leu Tyr Ile Pro Ser
aac c
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                                                                       120
agggaactcg agagcarcny cc atg ggc aca cag gag ggc tgg wgc ctg ctg
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                          Met Gly Thr Gln Glu Gly Trp Xaa Leu Leu
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ctc tgc ctg gct cta tct gga gca gca gaa acc aag ccc cac cca gca
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Leu Cys Leu Ala Leu Ser Gly Ala Ala Glu Thr Lys Pro His Pro Ala
    -10
                         -5
gag ggg cag tgg cgg gca gtg gdc gtg gtc cta gac ygt ttc ctg gtg
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Glu Gly Gln Trp Arg Ala Val Xaa Val Val Leu Asp Xaa Phe Leu Val
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                                     15
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Lys Asp Xaa Ala His Arg Gly Ala Leu Ala Ser Ser Glu Asp Arg Ala
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agg
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Arg
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32 cag tee tte tea ggg gte tee teg agg tte agt gge agt gga tet ggg Gln Ser Phe Ser Gly Val Ser Ser Arg Phe Ser Gly Ser Gly 60 aca gat ttc acc ctc aca atc aat agc ctg gaa cct ggg 331 Thr Asp Phe Thr Leu Thr Ile Asn Ser Leu Glu Pro Gly <210> 45 <211> 520 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 176..520 <221> sig_peptide <222> 176..235 <223> Von Heijne matrix score 11.1999998092651 seq AFLLLVALSYTLA/RD <400> 45 gaagataatc acttggggaa aggaaggttc gtttctgagt tagcaacaag taaatgcagc 60 actagtgggt gggattgagg tatgccctgg tgcataaata gagactcagc tgtgctggca 120 cactcagaag cttggaccgc atcctagccg ccgactcaca caaggcagag ttgcc atg 178 -20 gag aaa att cca gtg tea gea tte ttg ete ett gtg gee ete tee tae 226 Glu Lys Ile Pro Val Ser Ala Phe Leu Leu Val Ala Leu Ser Tyr -15 -10 act ctg gcc aga gat acc aca gtc aaa cct gga gcc aaa aag gac aca 274 Thr Leu Ala Arg Asp Thr Thr Val Lys Pro Gly Ala Lys Lys Asp Thr 1 aag gac tot ega eee aaa etg eee eag ace ete tee aga ggt tgg ggt 322 Lys Asp Ser Arg Pro Lys Leu Pro Gln Thr Leu Ser Arg Gly Trp Gly gac caa ctc atc tgg act cag aca tat gaa gaa gct cta tat aaa tcc 370 Asp Gln Leu Ile Trp Thr Gln Thr Tyr Glu Glu Ala Leu Tyr Lys Ser 30 35 40 aag aca agc aac aaa ccc ttg atg att att cat cac ttg gat gag tgc 418 Lys Thr Ser Asn Lys Pro Leu Met Ile Ile His His Leu Asp Glu Cys 50 55 cca cac agt caa gct tta aag aaa gtg ttt gct gaa aat aaa gaa atc 466 Pro His Ser Gln Ala Leu Lys Lys Val Phe Ala Glu Asn Lys Glu Ile 65 70 cag aaa ttg gca gag cag ttt gtc ctc ctc aat ctg gtt tat gaa aca 514 Gln Lys Leu Ala Glu Gln Phe Val Leu Leu Asn Leu Val Tyr Glu Thr 85 90 act gac 520 Thr Asp 95 <210> 46 <211> 383 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 25..381

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WO 99/53051

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tee etc atc tge ggt gte tet ggt gat tee gte acc att agt ggt tgg

Ser Leu Ile Cys Gly Val Ser Gly Asp Ser Val Thr Ile Ser Gly Trp

20

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Phe Phe Leu Leu Val Ala Ala Pro Arg Trp Val Leu Ser Gln Val
                -10
                                    -5
cag ctg cag gag tcg ggc cca gga ctg gtg aag cct tcg kwg acc ctg
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Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Xaa Thr Leu
                            10
tee etc acc tge act gte tet ggt gae tee atc agt agt tac tac tgg
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Ser Leu Thr Cys Thr Val Ser Gly Asp Ser Ile Ser Ser Tyr Tyr Trp
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age tgg ate egg cag eee eea ggg aag gga etg gag tgg att gge tat
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Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile Gly Tyr
                                        45
atc tat tac agt ggg agc acc aac tac aac ccc tcc ctc aag agt cga
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Ile Tyr Tyr Ser Gly Ser Thr Asn Tyr Asn Pro Ser Leu Lys Ser Arg
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gtc acc ata tca gtg gac acg tcc aag aac caa ttc tcc ctg aag ctg
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Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe Ser Leu Lys Leu
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age tet gtg ace gca gcg gac acg gcc gtg tat tac tgt gcg aga sgg
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Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Arg Xaa
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ctg cma tac tat gat agg agt ggt tat ttc aga tat ttt gac tac tgg
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ctc acc tgc aca gtc tct ggt ggc tcc atc gac agt ggt aat tac tac Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Asp Ser Gly Asn Tyr Tyr 20 25 30 35	199												
tgg agc tgg atc cgg cag ccc gcc ggg aag gga ctg gag tgg att ggg Trp Ser Trp Ile Arg Gln Pro Ala Gly Lys Gly Leu Glu Trp Ile Gly 40 45 50	247												
Arg Ile Tyr Ser Thr Gly Ser Thr Asn Tyr Asn Pro Ser Leu Ser Ser 55 60 65	295												
cga gtc cag ata tcg tta gac acg tcc aag aac ctg ctc tcc ttg aac Arg Val Gln Ile Ser Leu Asp Thr Ser Lys Asn Leu Leu Ser Leu Asn 70 75 80	343												
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acc ttc ccc ttc tac tgg tac ctc gat ctc tgg ggc cgt ggc atc ctg Thr Phe Pro Phe Tyr Trp Tyr Leu Asp Leu Trp Gly Arg Gly Ile Leu 100 105 110 115	439												
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ctg cag gag tcg ggc cca aga ctg gtg aag cct tca cag acc ctg tcc 151

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Trp	Ser	Trp	Ile	Arg	Gln	His	Pro	Gly	Arg	Gly	Leu	Glu	Trp	Ile 50	Gly	
tac	atc	tat	tac	aat	tgg	agc	acc	tac	tac	aat	ccg	tcc	ctc	agg	agt	295
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cga	gtt	acc	atg	tca	atg	gac	acg	tct	aag	aac	cag	ttc	tcc	ctg	aac	343
Arg	Val	Thr 70	Met	Ser	Met	Asp	Thr	Ser	Lys	Asn	Gln	Phe 80	Ser	Leu	Asn	
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qqt		gga	cgc	ctt	ggc	tgg	ttc	ash	mct	tng	ggg	mca	999	rac	cca	439
														Xaa		
100					105					110					115	
					agc											466
Gly	His	Arg	Leu		Ser	Arg	Pro	Gly								
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	> '52															
	.> 39															•
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4413	> nc	JIIO S	apro	-110												
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Met	цуз	1113	БСи	-15	riic	rnc	Deu	Deu	-10	vui	Alu	ALU	110	-5	112	•
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Val	Leu	Ser	Gln 1	Val	Gln	Leu	Gln 5	Glu	Ser	Gly	Pro	Gly 10	Leu	Val	Lys	
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	15					20					25	1	- 3			
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_	Thr	Gly	Ser	Tyr	-	Trp	Thr	Trp	Val		Gln	Pro	Pro	Gly		
30					35					40				.	45	200
														tac		298
отА	Leu	GIU	rrb	50	GIA	TAL	116	TAL	1yr 55	TIIT	GIY	vəħ	TIIT	Tyr 60	1 Y L	
aac	ccq	tcc	ctc	_	agt	cga	att	acc		tcr	cta	gac	acg	tny	wag	346
														Xaa		

55	
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ccctatgtc atg tca cct gtc ctc ttg gtg ctg tca ttg tca caa tgc ctt Met Ser Pro Val Leu Leu Val Leu Ser Leu Ser Gln Cys Leu -15 -10 -5	231
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	> CI	os)3:	18												•
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-400	> 55	:													
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											gtc Val				102
											cct Pro				150
			_	-	_			_		_	act Thr 30				198
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			gcg					gtg			tcg Ser 15	gcc			152
	acc					ggt					aat Asn				200

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Phe Leu Leu Val Ala Ala Pro Arg Trp Val Leu Ser Gln Val Gln
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                                                                       151
Leu Gln Glu Ser Gly Ser Gly Pro Val Asp Xaa Xaa Gln Thr Leu Xaa
                        10
etc acc tgc act gks tct ggt gtc tcc atc agc agt agt gat aat tgt
                                                                       199
Leu Thr Cys Thr Xaa Ser Gly Val Ser Ile Ser Ser Ser Asp Asn Cys
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tgg agc tgg atc cgg cag cca cca ggg aag ggc ctg gag tgg att gga
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Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile Gly
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Tyr Ile Tyr His Ser Gly Gly Thr Tyr Tyr Asn Pro Thr Leu Lys Ser
            55
                                60
ega gte ace ate teg gba gae agg ate agg aac caa tte tee etg aag
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Arg Val Thr Ile Ser Xaa Asp Arg Ile Arg Asn Gln Phe Ser Leu Lys
        70
                            75
ctg agc tct gtg acg gcc gyg gac acg gcc gtg tat kac tgt ggc aga
                                                                       391
Leu Ser Ser Val Thr Ala Xaa Asp Thr Ala Val Tyr Xaa Cys Gly Arg
                        90
gca cag ggt aga atg ggg atc ggg acg acg att ttt gat ctc tgg ggc
                                                                       439
Ala Gln Gly Arg Met Gly Ile Gly Thr Thr Ile Phe Asp Leu Trp Gly
100
                    105
ggg gga caa tgg tca ccg tct ctg cag cct
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Gly Gly Gln Trp Ser Pro Ser Leu Gln Pro
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      seq ILFLVAAATGAHS/QV
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<222> 210

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WO 99/53051 43 acc aac ttg gca aaa gac cta 348 Thr Asn Leu Ala Lys Asp Leu <210> 61 <211> 457 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 55..456 <221> sig_peptide <222> 55..111 <223> Von Heijne matrix score 10.8000001907349 seq ILFLVAAATGAHS/QV <400> 61 acccaaaaac cacaccctc cttgggagaa tcccctagat cacagctcct cacc.atg ' 57 gac tgg acc tgg agc atc ctt ttc ttg gtg gca gca gcg aca ggt gcc 105 Asp Trp Thr Trp Ser Ile Leu Phe Leu Val Ala Ala Ala Thr Gly Ala -15 -10 cac tee cag gtt cag etg gtg cag tet gga ggt gag gtg aag aag eet 153 His Ser Gln Val Gln Leu Val Gln Ser Gly Glu Val Lys Lys Pro ggg gcc tcc gtc aag gtc tcc tgc aag gct tct ggt tac acc ttt acc 201 Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr aga tat gat atc aac tgg gtg cga cag gcc cct gga caa ggg ctt gag 249 Arg Tyr Asp Ile Asn Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu tgg atg gga tgg atc agc gct dcc aat ggt aac aca aat tat gca cag 297 Trp Met Gly Trp Ile Ser Ala Xaa Asn Gly Asn Thr Asn Tyr Ala Gln 345

daa gtc cag ggc aga gtc acc atg acc aca gac aca tcc acg aga aca Xaa Val Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Arq Thr

393

457

gcc tac atg gaa ctg agg agc ctg cga tct gac gac acg gcc att tat Ala Tyr Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Ile Tyr

tac tgt gcg cga gag atm bta gtg gba sta tgt gat gga cag ttg ggg 441 Tyr Cys Ala Arg Glu Ile Xaa Val Xaa Xaa Cys Asp Gly Gln Leu Gly

95 cca ggg aac ctg gtc a Pro Gly Asn Leu Val

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<211> 439

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			ctc Leu													98
gag			cgg Arg 5												acc Thr	146
			acc Thr										ggt			194
		tgg	atc Ile				cca					gag				242
	atc		cac His	_		agc					ccg			_	_	290
cgc			ctc Leu		gtt					gac					agg	338
_			gtg Val 85	acc	-		-	_	gct				_	gcg	_	386
			gat Asp					tct					ttt			434
tgg Trp	9 9	100														439
<211 <212	0> 63 L> 23 2> D1 3> Ho	14 NA	sapie	ens		-										
	1> CI	DS 22:	13 .													
<22	2> 8: 3> Vo	2li on He core	eptio 26 eijno 10.0 LALF	e mai	9980		ı			•						
acc	_	gtg (tgtc:			atg	atg	ctt		gct	ttg	ttc	ttt	ttg		60 111
			ttg Leu			caa					ttc					159
aag			gtt Val 15						aag					att		207
	ggc Gly							-								214
-27	0	4														

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ce atq qae tgg ace tgg agg ate ete tte ttg gtg gea ger gee aca
                                                                       107
   Met Asp Trp Thr Trp Arg Ile Leu Phe Leu Val Ala Ala Ala Thr
                   -15
                                        -10
qqa qcc ctc tcc cag gtg cag ctg gtr cag tct gga ggt gar gtg aag.
                                                                       155
Gly Ala Leu Ser Gln Val Gln Leu Val Gln Ser Gly Gly Glu Val Lys
                1
                                 5
                                                                       203
aaq cet ggg gee tea gtg agg gte tee tge aag gee tet gga tae age
Lys Pro Gly Ala Ser Val Arg Val Ser Cys Lys Ala Ser Gly Tyr Ser
                            20
ttc atc ggc tat tat gta cac tgg ata cga cag act cct ggg cga sgc
                                                                       251
Phe Ile Gly Tyr Tyr Val His Trp Ile Arg Gln Thr Pro Gly Arg Xaa
                        35
                                             40
ctt qaq tgg atg ggg tgg gtc aac cct crs act ggc gac aac ggg g
                                                                       297
Leu Glu Trp Met Gly Trp Val Asn Pro Xaa Thr Gly Asp Asn Gly
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                                                                        60
gaccttgtgt ctttagtttg acctgtcctt cagtgagtgt atataaaatt ctaagctaaa
                                                                       120
acatattttc tgaaattgtg aaggtattgc atgtctatct tcttgcctac tctaaatata
tcaatcgttt tcttgggaag ttagtctttc tttcacactt gtctgtagat ctttac atg
                                                                       239
ttc ttt cag ttt tgg aag tcc tct gca tat tta ata ttt gtt agt att
                                                                       287
Phe Phe Gln Phe Trp Lys Ser Ser Ala Tyr Leu Ile Phe Val Ser Ile
                         -30
                                             -25
tgt aaa ggt tit cit cot gic tac cie cit cit git cie ict cie tet
                                                                       335
Cys Lys Gly Phe Leu Pro Val Tyr Leu Leu Leu Val Leu Ser Leu Ser
-20
                     -15
ctc tct ctc tgt tgc tct ctc ttg ctc tct ctc ca
                                                                       370
Leu Ser Leu Cys Cys Ser Leu Leu Leu Ser Leu
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<210> 66

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<222> 342..343
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                                                                        56
                                                  Met Asp Trp Thr
tgg agg atc ctc ttt ttg gtg gca gca gcc aca ggt gtc cac tcc cag
                                                                       104
Trp Arg Ile Leu Phe Leu Val Ala Ala Ala Thr Gly Val His Ser Gln
-15
                     -10
                                         -5
gtc cac ctt gtt cag tct ggg gct gar gtg aag aag cct ggg act ccg
                                                                       152
Val His Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Thr Pro
                                10
gtg aac att tcc tgt aag gct ttt ggc tac acc ttc cct gcc ttt gct
                                                                       200
Val Asn Ile Ser Cys Lys Ala Phe Gly Tyr Thr Phe Pro Ala Phe Ala
        20
ata cat tgg gtt cgc cag gcc ccc gga caa agt ctt gag tgg atg gga
                                                                       248
Ile His Trp Val Arg Gln Ala Pro Gly Gln Ser Leu Glu Trp Met Gly
                        40
                                             45
tgg gtc aac att ggc cat ggc aac aca aag tat tca cag aag ttt cag
                                                                       296
Trp Val Asn Ile Gly His Gly Asn Thr Lys Tyr Ser Gln Lys Phe Gln
50
                    55
                                         60
ggc aga ctc gcc atc tcc aga gac acg tcc gcg aac ata gtc tac nng
                                                                       344
Gly Arg Leu Ala Ile Ser Arg Asp Thr Ser Ala Asn Ile Val Tyr Xaa
                70
                                    75
gaa ctg agc ggc ctg aga tct gaa gac acg gct gtc tat tac tgt gcg
                                                                       392
Glu Leu Ser Gly Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala
            85
                                90
                                                     95
agg gat aat ett tte ttt gge agt atg gge ttt gae
                                                                       428
Arg Asp Asn Leu Phe Phe Gly Ser Met Gly Phe Asp
        100
                            105
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<222> 38..493
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												acc	tcc Ser			103
ctg Leu	Thr	Gln	Pro 10	Pro	tcg Ser	Val	Ser	Val 15	Ala	cca Pro	Gly	Lys	acg Thr 20	gcc Ala	Ser	151
													cac His			199
													gat Asp			247
													aac Asn			295
													gat Asp			343
													gga Gly 100			391
							_		_	_		_	gct Ala	_		439
													gcc Ala			487
gcc Ala 135																493
135 <210> 68 <211> 180 <212> DNA <213> Homo sapiens																
)> L> CI 2> 3(79									•				
<222	2> 36 3> Vo	on He	eijne 10.6	e mat	rix 00381 FSRQ/		7									
)> 68 cagtt		ccag	gctco	ec aa	atat	agat	att	1	let A		-	tg t Leu I	he I	Leu	53
									ggt				tct Ser	ctc		101
				ggt									agc Ser			149
		agc					tca	gcc Ala		a						180

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 <222> 38..259
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 <222> 38..94
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                                                                        55
                                          Met Lys His Leu Trp Phe
                                                           -15
 tte etc etc etg gtg tea get ecc aga tgg gte etg tet eag gtg eag
                                                                       103
 Phe Leu Leu Val Ser Ala Pro Arg Trp Val Leu Ser Gln Val Gln
 cta cag gag tog ggc cca gga ctg gtg aag cot tog ggg agg otg too
                                                                       151
 Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gly Arg Leu Ser
                         10
 ctc gcc tgc gat gtg gtg gaa ttg agt ccg ccg gcc ccc agg ggc ggg
                                                                       199
 Leu Ala Cys Asp Val Val Glu Leu Ser Pro Pro Ala Pro Arg Gly Gly
                     25
                                         30
 tot gca gtg cat ctc aga aat ctt tca tca tgg gag ccc cac cta caa
                                                                       247
 Ser Ala Val His Leu Arg Asn Leu Ser Ser Trp Glu Pro His Leu Gln
 ccc gtc tcg ggg
                                                                       259
 Pro Val Ser Gly
             55
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 <211> 178
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                                                                        48
        Met Thr Tyr Phe Pro Leu Gly Arg Tyr Pro Val Met Gly Leu
                -30
                                    -25
 ctg gat caa atg gta gtt gtg ttt tta ctt ctt tta gtc tcc aca ctt
 Leu Asp Gln Met Val Val Val Phe Leu Leu Leu Val Ser Thr Leu
 tot too gta gtg gtt tta ota gtt tgo att ooc acc ago agt gta aaa
                                                                       144
 Ser Ser Val Val Val Leu Leu Val Cys Ile Pro Thr Ser Ser Val Lys
 ttg ttc cct ttt cac cat atc cac acc aac tgg g
                                                                       178
 Leu Phe Pro Phe His His Ile His Thr Asn Trp
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. . 49

20 25 15 <210> 71 <211> 131 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 40..129 <221> sig_peptide <222> 40..96 <223> Von Heijne matrix score 10.5 seq WVLLVAMLRGLQC/QV <400> 71 agetetggga gacgageeca getetgeagt ggacteace atg gag ttt ggg etg Met Glu Phe Gly Leu age tgg gtt etc etc gtt get atg tta aga ggt etc eag tgt eaa gtg 102 Ser Trp Val Leu Leu Val Ala Met Leu Arg Gly Leu Gln Cys Gln Val -10 -5 cag ctg gtg gag tct ggg gga acc gcg gg 131 Gln Leu Val Glu Ser Gly Gly Thr Ala <210> 72 <211> 217 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 47..217 <221> sig_peptide <222> 47..91 <223> Von Heijne matrix score 10.5 seq LSLLILLENVSG/FP ttgcttacaa ttttaatgtg tctcattgct actggtcctc cttcta atg tat ctg 55 Met Tyr Leu age ttg tta att cta ctt ttg gaa aat gte agt gge ttt ccc ttt cct 103 Ser Leu Leu Ile Leu Leu Glu Asn Val Ser Gly Phe Pro Phe Pro -5 cta att ttc cag ctt cat gca tcc cct ggc cat aag ata ctt cca gac 151 Leu Ile Phe Gln Leu His Ala Ser Pro Gly His Lys Ile Leu Pro Asp 10 tgt atg ata tat tct atc act gtc agc ctt atg ttc cct gtg gtt gac 199 Cys Met Ile Tyr Ser Ile Thr Val Ser Leu Met Phe Pro Val Val Asp 30 35 tat ata agc acg caa ggg 217 Tyr Ile Ser Thr Gln Gly

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<211> 192

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                                                                        60
 gtttagatag ttgttaaatt tggtgttcct gtggggagg atg atg aga gcc ttc
                                                                       114
                                            Met Met Arg Ala Phe
 tat ttg gct atc ttg ttc tgc ctc tct ctc tcc tta tgg ttc tdk tgt
                                                                       162
 Tyr Leu Ala Ile Leu Phe Cys Leu Ser Leu Ser Leu Trp Phe Xaa Cys
             -20
                                -15
 tta ctt ttt ttg ctt ttt gct tgg cct ggg
                                                                       192
 Leu Leu Phe Leu Leu Phe Ala Trp Pro Gly
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                                                                        52
                          Met Ala Trp Thr Pro Leu Leu Phe Leu Thr
                          -20
                                              -15
 ctc ctc ctc cac tgc aca ggg tct ctc gcc cag ctt gtg ctg act caa
                                                                       100
Leu Leu Leu His Cys Thr Gly Ser Leu Ala Gln Leu Val Leu Thr Gln
                     -5
 teg ecc tet gee tet gee tee etg gga gee teg gte aag ete ace tge
                                                                       148
 Ser Pro Ser Ala Ser Ala Ser Leu Gly Ala Ser Val Lys Leu Thr Cys
 act ctg agc agt ggg cac agc aac tac ggc atc gct tgg tat cag cag
                                                                       196
 Thr Leu Ser Ser Gly His Ser Asn Tyr Gly Ile Ala Trp Tyr Gln Gln
                             30
 cag cca gag aag ggc cct cga ttc ttg atg aaa gtt aac agt gat ggc
                                                                       244
 Gln Pro Glu Lys Gly Pro Arg Phe Leu Met Lys Val Asn Ser Asp Gly
                         45
 age cae atg aag geg gae ggg ate eet gat ege tte tea gge tee age
                                                                       292
 Ser His Met Lys Ala Asp Gly Ile Pro Asp Arg Phe Ser Gly Ser Ser
                     60
 tct ggg gct gag cgc tac ctc tcc atc tcc agc ctc a
                                                                       329
 Ser Gly Ala Glu Arg Tyr Leu Ser Ile Ser Ser Leu
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70

394

aca gtc tac atg gag ctg agc agc ctg aca tct gac gac acg gcc gtg

Thr Val Tyr Met Glu Leu Ser Ser Leu Thr Ser Asp Asp Thr Ala Val

seq XLXLSVLLGXXXX/KX

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80
                            85
                                                 90
tat tat tgt gct aga gag gcg tat agt ggg agc tac cgc ttt gac tac
Tyr Tyr Cys Ala Arg Glu Ala Tyr Ser Gly Ser Tyr Arg Phe Asp Tyr
tgg gg
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Trp
110
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                Met Asp Leu Met Cys Lys Lys Met Arg His Leu Trp
                                         -20
ttc ctc ctc ctg ctg gtg gcg gct ccc aga tgg gtc ctg tcc cag ctg
                                                                       99
Phe Leu Leu Leu Val Ala Ala Pro Arg Trp Val Leu Ser Gln Leu
                                    -5
cag ctt cag gag tcg ggc cca gga ctg gtg aag gct tcg gag acc ctg
                                                                      147
Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Ala Ser Glu Thr Leu
                            10
tcc ctc gcc tgc agt gtc tct ggt gac tcc atc agc agt ggt aat tat
                                                                      195
Ser Leu Ala Cys Ser Val Ser Gly Asp Ser Ile Ser Ser Gly Asn Tyr
tac tgg ggc tgg atc cgg cag ccc cca ggg aag gga ctg cag tgg ctt
                                                                      243
Tyr Trp Gly Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Gln Trp Leu
                    40
                                        45
ggg agt ctt tgg aat cgt ggc ggt ccg caa tac aay hcc tcc ctc aag
                                                                      291
Gly Ser Leu Trp Asn Arg Gly Gly Pro Gln Tyr Asn Xaa Ser Leu Lys
                                    60
aat cga gtc acc gtg tcc gta gac acg tcc acg aat cat ttc ttt ctg
                                                                      339
Asn Arg Val Thr Val Ser Val Asp Thr Ser Thr Asn His Phe Phe Leu
                                75
aga ctg aat tcc gtg aay vgh gga cac ggc aat tta tta ctg tgc gcg a
                                                                      388
Arg Leu Asn Ser Val Asn Xaa Gly His Gly Asn Leu Leu Cys Ala
                            90
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Glu Gly Glu Ser Cys Val Glu Ser His Cys Val Leu Phe Phe Thr Leu	
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Met Glu Leu Gly Leu Ser Trp Leu Phe Leu Val -15 -10	
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Ala Phe Leu Lys Gly Val Gln Cys Glu Val Gln Leu Leu Glu Ser Gly	100
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	er Cys														
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 Met Asp Trp Thr Trp Arg Phe Leu Phe Val Val Ala Ala Ala Thr Gly
                  -15
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gtc cag tcc cag gtg cag ctg gtg cag tct ggg gct gag gtg aag aag
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Val Gln Ser Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys
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Pro Gly Ser Ser Val Lys Val Ser Cys Lys Ala Ser Gly Gly Thr Phe
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age and tat get ate age tgg gtg ega cag gee eet gga caa ggg ett
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Ser Xaa Tyr Ala Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu
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Glu Trp Met Gly Gly Ile Ile Pro Ile Phe Gly Thr Ala Xaa Tyr Ala
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Gln Lys Phe Gln Gly Arg Val Thr Ile Thr Ala Asp Xaa Ser Thr Xaa
aca rcc tac atg gag ctg agc agc ctg aga tct gag gac acg gcc stg
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Thr Xaa Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Xaa
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tat tac tgt gcg aga ggt caa gcc ccc ggt agg gta gta gta cca ctt
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Tyr Tyr Cys Ala Arg Gly Gln Ala Pro Gly Arg Val Val Pro Leu
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ttttgaataa gtaatamcat ybtacatggc ttaaaactga aaaacgtatt cctgttactt
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cttgatgctt ttgagaaatg aataatgttt tctccctttt aaatggtagt acagc atg
cac act ttt ctg tgc ttg ctt ttt tat ctc ata gta tct tgt gga gct
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His Thr Phe Leu Cys Leu Leu Phe Tyr Leu Ile Val Ser Cys Gly Ala
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                                          -35
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                                                                      101
Xaa Xaa Pro Pro Pro Leu Xaa Arg Xaa Ser Leu Pro Ala Cys Ala Asp
                -25
                                     -20
tca atc atc ctc tgm ctc tgm ttc cct ggg atc ctc ggw caa gct cac
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Ser Ile Ile Leu Xaa Leu Xaa Phe Pro Gly Ile Leu Gly Gln Ala His
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attattetea ccaaagatgt getteetgae etcaaaagee tgteageeta atataaagae
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agtgtgacaa atg cca atc ctg cct cag gac atc ttg cac ttg ctg atc
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           Met Pro Ile Leu Pro Gln Asp Ile Leu His Leu Leu Ile
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ctt ctg tct gga aca tgc ttc act tgg att ctt ttg tgg ctt cca ctc
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Leu Leu Ser Gly Thr Cys Phe Thr Trp Ile Leu Leu Trp Leu Pro Leu
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tcc cct ctg ttg ggc ctg aaa tgc ta
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  Met Lys Ala Leu Gly Ala Val Leu Leu Ala Leu Leu Cys Gly Arg
  ~20
                                          -10
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Pro Gly Arg Gly Gln Thr Gln Glu Glu Glu Glu Glu Asp Glu Asp
cac ggg cca gat gac tac gac gag gaa gat gag gat gag gtt gaa gag
                                                                      205
His Gly Pro Asp Asp Tyr Asp Glu Glu Asp Glu Val Glu Glu
gag gag acc aac agg ctc cct ggt ggc agg agc aga gtg ctg ctg cgg
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Glu Glu Thr Asn Arg Leu Pro Gly Gly Arg Ser Arg Val Leu Leu Arg
tgc tac acc tnk nag tcc ctg ccc agg gac gag cgc tgc aac ctg acg
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Cys Tyr Thr Xaa Xaa Ser Leu Pro Arg Asp Glu Arg Cys Asn Leu Thr
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agt tgg ttt cga cag acm ccg gag aag ggt ctg gag tgg att ggg gaa

Ser Trp Phe Arg Gln Thr Pro Glu Lys Gly Leu Glu Trp Ile Gly Glu

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<221> sig_peptide <222> 118..306

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	Glu	Trp	Leu	Gly		Ile	Ile	Pro	Ile		Gly	Ile	Thr	Asn	Tyr	Ala	
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															acg Thr		349
		-,-		65	,	9			70			p	-10	75		- 3	
															gcc		397
	Val	Val	-	Met	Glu	Gln	Ser		Leu	Thr	Ser	Ala	-	Thr	Ala	Val	
	+		80	~~~	222	ċ~~	2	85 25.0		+	a a -	a+-	90	a+-	+	+	445
															tac Tyr		445
	-,-	95	-,0		-, -	0	100				u	105	3		- , .	-,-	

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actcaactag tetttaatte etgttttgae aaactttata aggtgetaea agacag	
tttttcacca tctaccata atg tgg aac aga tat ttt gtc ttc tat ctc Met Trp Asn Arg Tyr Phe Val Phe Tyr Leu	ctg 172
-20 -15	
ctt ttg tca gcg ttt acg agt caa aca gta tcc gga caa aga aag a Leu Leu Ser Ala Phe Thr Ser Gln Thr Val Ser Gly Gln Arg Lys L	aa 220 ys
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Gly Pro Arg	230
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-1	
ttc ttc ctc ctg ctg gtg gca gct ccc aga tgg gtc ctg tcc cag c	
Phe Phe Leu Leu Val Ala Ala Pro Arg Trp Val Leu Ser Gln Leu -10 -5	
cag etc cag gag tec gge tea gga etg gag aag eet tea cag ace e	tg 150
Gln Leu Gln Glu Ser Gly Ser Gly Leu Glu Lys Pro Ser Gln Thr Lo 5 10 15	
tee etc acc tge tet gte tet ggt gge tee atc agt agt gat gat te	tg · 198
Ser Leu Thr Cys Ser Val Ser Gly Gly Ser Ile Ser Ser Asp Asp L 20 25 30	∍u ,
tog tgg ago tgg ato oga cag oog ooa ggg aag ggo otg gag tgg a	tt 246
Ser Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp I 35 40 45	
35 40 45 50	

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Xaa Ser Ser Lys Ser

Gly Tyr Ile Tyr Gln Asn Glu Arg Thr Leu Tyr Asn Pro Ser Leu Lys 55 60 agt cga gcc gcc att tca gtg gac agg tcc aag aac cag ttc tcc ctg 342 Ser Arg Ala Ala Ile Ser Val Asp Arg Ser Lys Asn Gln Phe Ser Leu aaa ctg acc tct gtg acc gcc gcg gac atg gcc gta tat tac tgt gcc 390 Lys Leu Thr Ser Val Thr Ala Ala Asp Met Ala Val Tyr Tyr Cys Ala 90 acc agt gtc atg awt tcc ttt ggg ggc gtt ctc gtc cct aat ctg ttt 438 Thr Ser Val Met Xaa Ser Phe Gly Gly Val Leu Val Pro Asn Leu Phe 105 ttg act act ggg gcc agg gaa tct cgt ca 467 Leu Thr Thr Gly Ala Arg Glu Ser Arg <210> 100 <211> 504 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 39..503 <221> sig_peptide <222> 39..95 <223> Von Heijne matrix score 9.30000019073486 seq FLLLVAGPRWVLS/QV <400> 100 aatactttct gagagtcctg gacctcctgt gcaagaac atg aaa cac ctg tgg ttc Met Lys His Leu Trp Phe ttc ctc ctg ctg gtg gca ggt ccc aga tgg gtc ctg tcc cag gtg cag 104 Phe Leu Leu Val Ala Gly Pro Arg Trp Val Leu Ser Gln Val Gln ctg sdk gag tcg ggc cca aga ctg gtg aag cct tca cag acc ctg tcc 152 Leu Xaa Glu Ser Gly Pro Arg Leu Val Lys Pro Ser Gln Thr Leu Ser 5 ctc acc tgc act gta tct ggg gcc tcc gtc agc agt cgt ggg tac tat 200 Leu Thr Cys Thr Val Ser Gly Ala Ser Val Ser Ser Arg Gly Tyr Tyr tgg acc tgg atc cgc cag ctc cca ggg aag ggc ctg gag tgg att ggc 248 Trp Thr Trp Ile Arg Gln Leu Pro Gly Lys Gly Leu Glu Trp Ile Gly 40 45 tac atc tgk tac act ggg agc acc ttc tac aac ccg tcc ctc aag agt 296 Tyr Ile Xaa Tyr Thr Gly Ser Thr Phe Tyr Asn Pro Ser Leu Lys Ser 60 cga tta acc ata tca ata gac acg tct aag aat cag ttc tcc ctg aac 344 Arg Leu Thr Ile Ser Ile Asp Thr Ser Lys Asn Gln Phe Ser Leu Asn 75 ctg agg tct gtg act acc gcg gac acg gcc gtc tat tac tgt gcg aga 392 Leu Arg Ser Val Thr Thr Ala Asp Thr Ala Val Tyr Tyr Cys Ala Arg 90 gac cat ttc gat ctt cta ttc gac ccc tgg ggc cag gga acc ctg gtc 440 Asp His Phe Asp Leu Leu Phe Asp Pro Trp Gly Gln Gly Thr Leu Val 105 110 acc gtc tcc tct gcm tcc acc aag ggc cca tcg gtc ttc ccc ctg gca 488 Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala 120 125 scc tcc tcc aag agc a 504

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gccaggcctg gaaggatgcg aggctcccgc tctccaccac aagcaacgaa gcctgcaagc
                                                                       120
tgttcgatgc cacgctgacc cagggta atg gcc tgc cga gag agg ccg cgc ccc
                                                                       174
                              Met Ala Cys Arg Glu Arg Pro Arg Pro
ctt ctg tgg agg tct agg gga agg ttt ttt aat tgg gga aag ctg ttt
                                                                      222
Leu Leu Trp Arg Ser Arg Gly Arg Phe Phe Asn Trp Gly Lys Leu Phe
        -30
                            -25
                                                 -20
ttt tgt ttt gtt ttg mtt ttg ttt tgt ttt gtt ttt gag gcg gag tct
                                                                      270
Phe Cys Phe Val Leu Xaa Leu Phe Cys Phe Val Phe Glu Ala Glu Ser
                        -10
cgc tet gtc gcc cag gct gga gtg cag tgg cgc tat ttc ggc tca cta
                                                                      318
Arg Ser Val Ala Gln Ala Gly Val Gln Trp Arg Tyr Phe Gly Ser Leu
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caa gct ttg cct ccc tgg
                                                                      336
Gln Ala Leu Pro Pro Trp
            20
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actttccaat tttcccagca ccatttattg gagaaactgt ctttttccca gtgcatgttc
                                                                      180
ttggcacctt tgttgaaaaa cagttggcca tag atg cat gaa ttt att tct ggg
                                                                      234
                                     Met His Glu Phe Ile Ser Gly
ttc ttt att ctc ttt cat tgg tct ctg tgt ttg tgt tta tgc caa tac
                                                                      282
Phe Phe Ile Leu Phe His Trp Ser Leu Cys Leu Cys Leu Cys Gln Tyr
cat gcc g
                                                                      289
His Ala
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                                                                      120
tcctttcatt tcatctcttg tccttcagtc attcctaaac attgacaybc attgagttcc
                                                                      180
ttggctctgg ccatagtcct ttctcccttt cccctctggg gcatcaaata gtgattacag
                                                                      240
tatecacagg g atg gea tat gee att tea eea ttt eac agt tee tgg aat
                                                                      290
             Met Ala Tyr Ala Ile Ser Pro Phe His Ser Ser Trp Asn
                     -40
                                          -35
cca ctt ttc act tct cat aaa gct tca gca agc cat tct cat ctt ggg
                                                                      338
Pro Leu Phe Thr Ser His Lys Ala Ser Ala Ser His Ser His Leu Gly
                -25
                                    -20
ttg ctt gtt tgc cta ttt gct gtt aca tcc att ctc tgc tcc tca
                                                                      383
Leu Leu Val Cys Leu Phe Ala Val Thr Ser Ile Leu Cys Ser Ser
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                                Met Ser Pro Val Leu Leu Leu Ala
                                -15
                                                     -10
ete etg ggg tte ate ete eea etg eea ggn agt gea rge get gss tek
                                                                      101
Leu Leu Gly Phe Ile Leu Pro Leu Pro Gly Ser Ala Xaa Ala Xaa Ser
        -5
                            1
gcc agt ttg gga cag ttc agc atg tgt gga agg tgt ccg acm tgc ccc
                                                                      149
Ala Ser Leu Gly Gln Phe Ser Met Cys Gly Arg Cys Pro Thr Cys Pro
                                        20
                    15
ggc aat gga ccc cta aga aca cca gct gcg aca sgg vtt rgg gtg cca
                                                                      197
Gly Asn Gly Pro Leu Arg Thr Pro Ala Ala Thr Xaa Xaa Xaa Val Pro
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35
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 gga cac gtt gat gc
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 Gly His Val Asp
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 ccg tgg tct tta ctg ctt ttc tcc ctg atg tgt gaa aca agc gcc ttc
                                                                       100
 Pro Trp Ser Leu Leu Phe Ser Leu Met Cys Glu Thr Ser Ala Phe
                     -10
 tat gtg cct ggg gtc gcg cct atc aac ttc cac cag aac gat ccc gta
                                                                       148
 Tyr Val Pro Gly Val Ala Pro Ile Asn Phe His Gln Asn Asp Pro Val
                                 10
 gaa atc aag gct gtg aag ctc acc agc tct cga acc cag cta cct tat
                                                                       196
 Glu Ile Lys Ala Val Lys Leu Thr Ser Ser Arg Thr Gln Leu Pro Tyr
 gaa tac tat tca ctg ccc ttc tgc cag ccc agc aag ata acc tac aag
                                                                       244
 Glu Tyr Tyr Ser Leu Pro Phe Cys Gln Pro Ser Lys Ile Thr Tyr Lys.
     35
                       · 40
 gca gag aat ctg gga gag gtg ctg aga ggg gac cgg att gtc aac acc
                                                                       292
 Ala Glu Asn Leu Gly Glu Val Leu Arg Gly Asp Arg Ile Val Asn Thr
 cct ttc cag gtt ctc atg aac agc gag aag tgt gaa gtt ctg tgc
                                                                       340
 Pro Phe Gln Val Leu Met Asn Ser Glu Lys Lys Cys Glu Val Leu Cys
                                     75
 age cag tee aac aag eea gtg ace etg aca gtg gag cag age ega ete
                                                                       388
 Ser Gln Ser Asn Lys Pro Val Thr Leu Thr Val Glu Gln Ser Arg Leu
                                 90
 gtg gcc gag cgg atc aca gaa gac tac tac gtc cac ctc att gct gac
                                                                       436
 Val Ala Glu Arg Ile Thr Glu Asp Tyr Tyr Val His Leu Ile Ala Asp
         100
                             105
 aac ctg cct gtg gcc acc ggc tgg agc tct act cca acc gag aca gcg
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. Asn Leu Pro Val Ala Thr Gly Trp Ser Ser Thr Pro Thr Glu Thr Ala
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                         120
                                              125
 atg aca ag
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 Met Thr
 130
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ctg atc tct ctt caa tgt gct cat gtg tcc ctt ggc tta cag tat
                                                                       103
Leu Ile Ser Leu Leu Gln Cys Ala His Val Ser Leu Gly Leu Gln Tyr
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cca tgc stt ctc ctt ctc cct cc
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Pro Cys Xaa Leu Leu Pro
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gacggctgct ggttttgaaa c atg aat ctt tcg ctc gtc ctg gct gcc ttt
                                                                      111
                        Met Asn Leu Ser Leu Val Leu Ala Ala Phe
                                -15
tgc ttg gga ata gcc tcc gct gtt cca aaa ttt gac caa aat ttg gat
                                                                      159
Cys Leu Gly Ile Ala Ser Ala Val Pro Lys Phe Asp Gln Asn Leu Asp
aca aag tgg tac cag tgg aag gca aca cac aga aga tta tat ggc gcg
                                                                      207
Thr Lys Trp Tyr Gln Trp Lys Ala Thr His Arg Arg Leu Tyr Gly Ala
10
                    15
aat gaa gaa gga tgg agg aga gca gcg tgg gag gg
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Asn Glu Glu Gly Trp Arg Arg Ala Ala Trp Glu
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gct at Ala Il								gtg	cag				tct	999 .	161
gga ga Gly As 10	p Leu														209
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ata ca Ile Hi															98
gta gt Val Va 15															146
pro Le			gg												160
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                                                                      113
                      Met Glu Leu Gly Leu Ser Trp Ile Phe Leu Leu
                                       -15
gct att tta aaa ggt gtc cag tgt gaa gtg cag ctg gtg gag tct ggg
                                                                      161
Ala Ile Leu Lys Gly Val Gln Cys Glu Val Gln Leu Val Glu Ser Gly
            - 5
gga ggc ttg gta cag cct ggc agg tcc ctg aga ctc tcc tgt gca gcc
                                                                      209
Gly Gly Leu Val Gln Pro Gly Arg Ser Leu Arg Leu Ser Cys Ala Ala
                        15
tot gga tto acc ttt gat gat tac gcc atg cac tgg gtc cgg caa gct
                                                                      257
Ser Gly Phe Thr Phe Asp Asp Tyr Ala Met His Trp Val Arg Gln Ala
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                                         35
cca ggg aag ggc ctg gag tgg gtc tca gga att act tgg aat agt ggt
                                                                      305
Pro Gly Lys Gly Leu Glu Trp Val Ser Gly Ile Thr Trp Asn Ser Gly
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                                    50
ann ata ggc tac gcg gac tct gtg aag ggc cga ttc acc atc tcc aga
                                                                      353
Xaa Ile Gly Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg
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gac aac gcc aag aac tcc ctg tat ttg caa atg aac agt ctg aga act
                                                                      401.
Asp Asn Ala Lys Asn Ser Leu Tyr Leu Gln Met Asn Ser Leu Arg Thr
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                            80
gag gac acg gcc ttc tat ttc tgt gca aaa gct cgc ggg ctc ttt agc
                                                                      449
Glu Asp Thr Ala Phe Tyr Phe Cys Ala Lys Ala Arg Gly Leu Phe Ser
                        95
                                             100
gat acc tgg ccc tac vnn cac tac gct atg gac gtc tgg ggc caa ggg
                                                                      497
Asp Thr Trp Pro Tyr Xaa His Tyr Ala Met Asp Val Trp Gly Gln Gly
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taccacaggg etetectge atg ete ett gtt tte ttt gtg ete tgg act tge
                                                                      112
                     Met Leu Leu Val Phe Phe Val Leu Trp Thr Cys
                                      -10
tca ctt gca ctg ctt gct tct tcc cca atc gcm gcc yac cca
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Ser Leu Ala Leu Leu Ala Ser Ser Pro Ile Ala Ala Xaa Pro
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atg gac tgg acc tgg aga atc ctc ctc ttg gtg gca gca gcc aca gat
                                                                      106
Met Asp Trp Thr Trp Arg Ile Leu Leu Leu Val Ala Ala Ala Thr Asp
                -15
                                    -10
gee tee tee cag atg cag etg ttg cag tet ggg eet gaa gtg aag aag
                                                                      154
Ala Ser Ser Gln Met Gln Leu Leu Gln Ser Gly Pro Glu Val Lys Lys
act ggg tcc tca gtg aaa ctt tcc tgc acg gcc tcc ggc gac acc ctc
                                                                      202
Thr Gly Ser Ser Val Lys Leu Ser Cys Thr Ala Ser Gly Asp Thr Leu
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gcc tac cac tac ctg cac tgg gtg cga cag gcc ccc gga caa gcg ctt
                                                                      250
Ala Tyr His Tyr Leu His Trp Val Arg Gln Ala Pro Gly Gln Ala Leu
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gag tgg atg gga tgg atc aca cct ttc agt gga gac acc aac ttc gca
                                                                      298
Glu Trp Met Gly Trp Ile Thr Pro Phe Ser Gly Asp Thr Asn Phe Ala
                50
cag cga ttc cag gac aga ctc acc ttc acc agg gac agg tct atg agc
                                                                      346
Gln Arg Phe Gln Asp Arg Leu Thr Phe Thr Arg Asp Arg Ser Met Ser
            65
                                70
aca gtc tac atg acc ctg acc agc ctg ata tct gaa gac aca gcc atg
                                                                      394
Thr Val Tyr Met Thr Leu Thr Ser Leu Ile Ser Glu Asp Thr Ala Met
        80
                            85
tat tac tgt gcc act gat gga cgt cgc acc aac cgt ctt ttt gaa ca
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Tyr Tyr Cys Ala Thr Asp Gly Arg Arg Thr Asn Arg Leu Phe Glu
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-15 ttg ctg gga tgc ctg ctt tgg ctg ctc acc cac att aaa gcc cag gac Leu Leu Gly Cys Leu Leu Trp Leu Leu Thr His Ile Lys Ala Gln Asp -10 -5	223
tca gtc agg gat gcc tac tgg aag act ggt agc tgc cca cct cca ttt Ser Val Arg Asp Ala Tyr Trp Lys Thr Gly Ser Cys Pro Pro Pro Phe 5 10 15	271
ctc cat gtg tct acc ttc nnn kkt aaa ctt acc ttc tcc act aag ggc Leu His Val Ser Thr Phe Xaa Xaa Lys Leu Thr Phe Ser Thr Lys Gly 20 25 30	319
aac ctt ctg cat tcc att cct ctc tct tcc ccc tta gcc tgt gtt ctt Asn Leu Leu His Ser Ile Pro Leu Ser Ser Pro Leu Ala Cys Val Leu 35 40 45 50	367
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acg ccg ccg gaa aac ctg att ggc gcc ctc ttg gcg atc ttc ggg cac Thr Pro Pro Glu Asn Leu Ile Gly Ala Leu Leu Ala Ile Phe Gly His -60 -55 -50	148
ctc gtg gtc agc att gca ctt aac ctc cag aag tac tgc cac atc cgc Leu Val Val Ser Ile Ala Leu Asn Leu Gln Lys Tyr Cys His Ile Arg -45 -40 -35	196
ctg gca ggc tcc aag gat ccc cgg gcc tat ttc aag acc aag aca tgg Leu Ala Gly Ser Lys Asp Pro Arg Ala Tyr Phe Lys Thr Lys Thr Trp -30 -25 -20	244
tgg ctg ggc ctg ttc ctg atg ctt ctg ggc gag ctg ggt gtg ttc gcm Trp Leu Gly Leu Phe Leu Met Leu Leu Gly Glu Leu Gly Val Phe Ala -15 -10 -5	292
ton tac goo tto gog dog dtg toa oto ato gtg doc oto ago	334

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292

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actgaaactt tctgcttgag ctcttgtttt gccaggctga tggggctgag gtgcaccctc
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tgaggaaaag ctgtaaatac atg gat ttt acc caa tgc cat tcc ctt ctt tta
                      Met Asp Phe Thr Gln Cys His Ser Leu Leu Leu
                      -35
                                          -30
agg gtt gaa tat tot coa gtg tot gto tgc ttt tta tta ctt tcc gtt
                                                                      221
Arg Val Glu Tyr Ser Pro Val Ser Val Cys Phe Leu Leu Ser Val
                -20
                                    -15
gcc ttc aat cag ttg gtt ttt gct ttg tat cca ata caa gct acw btc
                                                                      269
Ala Phe Asn Gln Leu Val Phe Ala Leu Tyr Pro Ile Gln Ala Thr Xaa
tgt ttc tct dda gtt tct ctc cct ttc ccc gct ca
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Cys Phe Ser Xaa Val Ser Leu Pro Phe Pro Ala
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                                                                      111
                Met Leu Leu Leu Leu Ala Cys Gly Val Pro Ser
                 -15
                                     -10
ctg tgg ccc ttt gcw ctt gct ctc tta aag acc c
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Leu Trp Pro Phe Ala Leu Ala Leu Leu Lys Thr
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atttggtttg ccagtatttt gttaaggatt tttacatca atg ttc att gag aat 174
Met Phe Ile Glu Asn

et Phe lie Glu A

205

386

cta tca aga cga gct ggt acc att cct act gaa aca att cca aaa aaa 270
Leu Ser Arg Arg Ala Gly Thr Ile Pro Thr Glu Thr Ile Pro Lys Lys

ttg agg agg aga gac ggg
Leu Arg Arg Arg Asp Gly

Leu arg arg arg asp Gly 15 20

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aggtgcaagg atg cag aac aga act gge ete att ete tgt get ytt gee 109
Met Gln Asn Arg Thr Gly Leu Ile Leu Cys Ala Xaa Ala
-20

ctc ctg atg ggt ttc ctg atg gtc tgc ctg ggg gcc ttc ttc att tcc

157
Leu Leu Met Gly Phe Leu Met Val Cys Leu Gly Ala Phe Phe Ile Ser

tgg ggc tcc ata ttc gac tgt cag ggg agc ctg att gcg gcc tat ttg

Trp Gly Ser Ile Phe Asp Cys Gln Gly Ser Leu Ile Ala Ala Tyr Leu
10 15 20

ctt ctg cct ctg ggg ttt gtg atc ctt ctg agt gga att ttc tgg agc 253
Leu Leu Pro Leu Gly Phe Val Ile Leu Leu Ser Gly Ile Phe Trp Ser
25 30 35

aac tat cgc cag gtg act gaa agc aaa gga gtg ttg agg cac atg ctc 301

Asn Tyr Arg Gln Val Thr Glu Ser Lys Gly Val Leu Arg His Met Leu 40 45 50

cga caa cac ctt gct cat ggg gcc ctg ccc gtg gcc aca gta gac agt
Arg Gln His Leu Ala His Gly Ala Leu Pro Val Ala Thr Val Asp Ser

55 60 65 gct gct ctt ctg aaa atc atg tgt aag car ttg ctt t

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aag ctg tat cga ttg ttg aga tct ggc gac ttg ttt aaa ttt cat cag
                                                                       102
Lys Leu Tyr Arg Leu Leu Arg Ser Gly Asp Leu Phe Lys Phe His Gln
                            -30
        -35
                                                -25
cet cac tte tat gaa ete tea gge ete aeg tgt ace age tet etg ete
                                                                       150
Pro His Phe Tyr Glu Leu Ser Gly Leu Thr Cys Thr Ser Ser Leu Leu
                         -15
                                             -10
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Ser Phe Ala Leu Gly Arg Ser Ile Pro Gly Ser Phe Pro
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                                                                       100
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Leu Leu Phe Ser Gly Ala Val Ala Leu Ile Gln Thr Trp Ala Gly Glu
tgc ggg gtc ggg agg gaa aag gcc tct gcg gga agg agc gag ggg ccc
                                                                       148
Cys Gly Val Gly Arg Glu Lys Ala Ser Ala Gly Arg Ser Glu Gly Pro
                     10
                                         15
gcc cgg agg agt aaa tct gca cat ata kbt aat tac aga tta caa tta
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Ala Arg Arg Ser Lys Ser Ala His Ile Xaa Asn Tyr Arg Leu Gln Leu
caa tca agg cag ggg
Gln Ser Arg Gln Gly
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ggaaacncaa gaggtggttt ttgtttttta aaacttctgt ttcttgggag ggggtgtggc
                                                                      240
ggggcagg atg agc aac tcc gtt cct ctg ctc tgt ttc tgg agc ctc tgc
                                                                      290
         Met Ser Asn Ser Val Pro Leu Leu Cys Phe Trp Ser Leu Cys
             -15
                                 -10
tat tgc ttt gct gcg ggg agc ccc gta cct ttt ggt cca gag gga cgg
                                                                      338
Tyr Cys Phe Ala Ala Gly Ser Pro Val Pro Phe Gly Pro Glu Gly Arg
ctg gaa gat aag ctc
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Leu Glu Asp Lys Leu
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                                                                       60
cageeggatt teccagecaa acgeagagag ag atg eec tgg ace ate ttg etc
                                    Met Pro Trp Thr Ile Leu Leu
                                                                      161
ttt gca gct ggc tcc ttg gcg atc cca gca cca tcc atc cgg gtg gtg
Phe Ala Ala Gly Ser Leu Ala Ile Pro Ala Pro Ser Ile Arg Val Val
ccc ccg tac cca agc agc caa gag gac ccc atc cac atc gca tgc atg
                                                                      209
Pro Pro Tyr Pro Ser Ser Gln Glu Asp Pro Ile His Ile Ala Cys Met
gcc gct ggg aac ttc ccg ggg gcg aat ttc aca ctg tat c
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score 8.39999961853027

									80)							
	cct Pro																330
	g ggt i Gly 25	ttt					art					Ser					378
tta Lei	a ayg ı Xaa	ggr Gly	gtt Val	ccc Pro	cca Pro 45	gag	gtt Val	ang Xaa	gaa Glu	ctc Leu 50	cct	ttc	ttt Phe	cca Pro	tat Tyr 55		426
	agc Ser											•	•			•	437
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	g gaa r Glu							acc	tgg				cac	tcc			101
	g tat s Tyr	ttc												Pro			149
	c atc e Ile																197
cg Ar	g gag g Glu	aca Thr	cgg Arg 45	agc Ser	gcc Ala	agg Arg	gac Asp	acc Thr 50	gca Ala	cag Gln	att Ile	ttc Phe	cga Arg 55	gtg Val	aac Asn		245
ct Le	g cgg u Arg	acg Thr 60	ctg Leu	cgc Arg	ggc Gly	tac Tyr	tac Tyr 65	aat Asn	cag Gln	agc Ser	gag Glu	gcc Ala 70	Gly 999	tct Ser	cam Xaa		293
	c ctg r Leu 75	_	_														304
<2 <2	10> 1 11> 2 12> I 13> H	44 NA	sapi	ens													,
<2	20> 21> 0 22> 1		43														
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                                                                      120
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        Met Cys Arg Ala Ala Cys Ile Ile Arg Met Ala Val Arg Ile
                    -30
                                        -25
tca ttc ttt ctt tct tac cat gct ctg tct ctc tgc ctt tgt aca tgt
                                                                      217
Ser Phe Phe Leu Ser Tyr His Ala Leu Ser Leu Cys Leu Cys Thr Cys
                -15
gcg ttt gca ttt ctc tcc ctc ggg
                                                                      244
Ala Phe Ala Phe Leu Ser Leu Leu Gly
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                                           Met Lys Phe Leu Leu
ctg gma gcc ctc gga ttc ctg amc cag gtg aat ccc arc cca att sma
                                                                      102 -
Leu Xaa Ala Leu Gly Phe Leu Xaa Gln Val Asn Pro Xaa Pro Ile Xaa
ggd ggg tca aaa atg tgt gag twa cac ccc agg ata ctg cag gac atg
                                                                      150
Gly Gly Ser Lys Met Cys Glu Xaa His Pro Arg Ile Leu Gln Asp Met
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                                        15
ttg cca ctg ggg gga gac agc att gtt cat gtg caa cgc tks cag aaa
                                                                      198
Leu Pro Leu Gly Gly Asp Ser Ile Val His Val Gln Arg Xaa Gln Lys
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atg ctg cat cag yta ctc c
                                                                      217
Met Leu His Gln Leu Leu
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       seq SILLLLAPPLPSA/VS
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 <222> 189
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cagagettet tegaettate etgeeteece taetttaatt etgttaaagt agttgaacae
                                                                       120
cattettete ataatagtte teectesatt etteagtgat tyeettgtgt ttataggata
aagtccacnt gttattttgg cagtcagttc aagatccaca aatcagtctt tacccttaca
teettattte teactgetgt tetaatatag tetttatace agteaggetg gtetgtteae
tattcctga atg ttt ttc tcc att ctt ttg tta ttg gca ccc ccg cta ccc
          Met Phe Phe Ser Ile Leu Leu Leu Leu Ala Pro Pro Leu Pro
               -15
                                   -10
tet gea gtg tet ttg eta eet tte ttt tte tae tgt gtg eag gg
                                                                       395
Ser Ala Val Ser Leu Leu Pro Phe Phe Phe Tyr Cys Val Gln
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<221> sig_peptide
<222> 141..206
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caactctgct gttttgtagg aagccacatg gaggtcattt acggttacta gttatcttag
tcagcttggg cagccattaa aaaataatac tgtagacgga gtggcccaaa cgagagaaat .
                                                                       120
ttatttctta tagttttggc atg gta gat ttc atc ctg agg tct ctt ctc ttg
                                                                       173
                      Met Val Asp Phe Ile Leu Arg Ser Leu Leu Leu
                               -20
gtt tgt agt tgg ctg tca atc tcc ctg cat gct cac acg acc gct ttt
                                                                       221
Val Cys Ser Trp Leu Ser Ile Ser Leu His Ala His Thr Thr Ala Phe
                         -5
tgt aca tac agt aag aaa ata cac act gtc atg tca ttt ttt tgt aa
Cys Thr Tyr Ser Lys Lys Ile His Thr Val Met Ser Phe Phe Cys
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87 <211> 170 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 93..170 <221> sig peptide <222> 93..140 <223> Von Heijne matrix score 8.10000038146973 seq LLYFLCVSSYVTS/FF ttttgactga tatcaaattc taggtggacc gagattttct ttcagtcttt caaagatatt 60 actotattgc cttctatctt gcatagtttc tg atg aga agt ctg ttg tat ttc 113 Met Arg Ser Leu Leu Tyr Phe -15 tta tgt gtt tct tca tat gta aca tct ttt ttc ttt ttt ttt ttt 161 Leu Cys Val Ser Ser Tyr Val Thr Ser Phe Phe Phe Phe Phe Phe ttt ttt ttt 170 Phe Phe Phe 10 <210> 141 <211> 396 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 192..395 <221> sig_peptide <222> 192..236 <223> Von Heijne matrix score 8 seq FISFLCLIALAGT/SS <400> 141 gattctcagc ttagttgctg ttggtgtata ggagagctac tgatttgtgt acattaattt tgtatccgga aactttgttg aattatttta tcagttctag gagctttttg gaggagtctt 120 tagggttctc taggtataca atcatatcat cagcaaacag tgacaattcg acttcctctt 180 tatggatttg t atg ccc ttt att tct ttc ctt tgt ctg att gct ctg gct 230 Met Pro Phe Ile Ser Phe Leu Cys Leu Ile Ala Leu Ala -10 ggg act tcc agt act atg ttg aga agt gct ctg gct ggg act tcc agt 278 Gly Thr Ser Ser Thr Met Leu Arg Ser Ala Leu Ala Gly Thr Ser Ser act atg tkg arg aga agt ggt gam agt ggg wat cct kgh ctk gty cma 326 Thr Met Xaa Xaa Arg Ser Gly Xaa Ser Gly Xaa Pro Xaa Leu Val Xaa 25 20 gtc ctm aga ggg aat gct ttc agc ttt ttc cca ttc agt ctg atg twg 374 Val Leu Arg Gly Asn Ala Phe Ser Phe Phe Pro Phe Ser Leu Met Xaa 35

396

<210> 142 <211> 357

gct atg ggt tgt cat aga tgg c Ala Met Gly Cys His Arg Trp

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       seq FLLGAIFIALSSS/RI
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                                                                        60
 tgttctgcaa taggcggctt agagggaggg gctttttcgc ctatacctac tgtagcttct
                                                                       120
ccacgtatgg accetaaagg ctactgetge tactaegggg ctagacagtt actgteteag
                                                                       180
ctctaggatg tgcgttcttc cactagaagc tcttctgagg gaggtaatta aaaaacagtg
                                                                       240
gaatggaaaa acagtgctgt agtcatcctg taatatgctc cttgtcaaca a atg tat
                                                                       297
aca ttc ctg cta ggt gcc ata ttc att gct tta agc tca agt cgc atc
                                                                       345
Thr Phe Leu Leu Gly Ala Ile Phe Ile Ala Leu Ser Ser Ser Arg Ile
tta cta gtg aag
                                                                       357
Leu Leu Val Lys
<210> 143
 <211> 159
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<222> 26..157
<221> sig_peptide
<222> 26..151
<223> Von Heijne matrix
      score 7.90000009536743
      seq LVCVCVCVCVCXC/XR
<400> 143
tgtgtgtgtg tgtgtctgcg tgtgt atg tgt ttg tgt ccc tgc tgg gat gtg
                                                                        52
                            Met Cys Leu Cys Pro Cys Trp Asp Val
                                     -40
                                                         -35
ttt act gtg ttt gtg tgt gtc tct gtg tgt gtg tct gtg tct gtc cct
                                                                       100
Phe Thr Val Phe Val Cys Val Ser Val Cys Val Ser Val Ser Val Pro
            -30
                                 -25
gtc ggg atg tat tta gtg tgt gtg tgt gtg tgt gtg tgt gtg tgt stc
                                                                       148
Val Gly Met Tyr Leu Val Cys Val Cys Val Cys Val Cys Xaa
        -15
                             -10
tgc gyg cgt gg
                                                                       159
Cys Xaa Arg
    1
<210> 144
<211> 433
<212> DNA
<213> Homo sapiens
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89
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<222> 282..431
<221> sig_peptide
<222> 282..383
<223> Von Heijne matrix
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      seq LFSLLMLTQSPLA/GQ
<221> misc feature
<222> 132,149
<223> n=a, g, c or t
<400> 144
aaaataaggt atctggcaaa agaatatatg aaagagtatg aagaactctc cttgaaagct
                                                                       60
gtggccccca ttggccatgg ctgcagagcc gatgtcccgg ccaatccagg cgggatcccc
                                                                      120
ttgaagcmgg knsmwhbtcy kragscwknc cmabtctccg ggggcaastc ttttcccttc
                                                                      180
cctgtgaccc kcttcggaca gttgaccatc tcaacaccta gtggttaaaa agaagagcat
                                                                      240
ggacggcctg gggcctgcac tggctgtgct gggagtttgt c atg ttg ata gct aag
                                                                      296
                                               Met Leu Ile Ala Lys
cag gcc cag ccc caa ggc ctc act gcc atc tgc ttc cct ctc aca cct
                                                                      344
Gln Ala Gln Pro Gln Gly Leu Thr Ala Ile Cys Phe Pro Leu Thr Pro
                -25
                                     -20
ctc ttc tcc ctc ctc atg ctc act cag agc ccc ctt gca ggt cag gaa
                                                                      392
Leu Phe Ser Leu Leu Met Leu Thr Gln Ser Pro Leu Ala Gly Gln Glu
            -10
                                 -5
gga aga gga ggg aaa gaa cgg tac ttg ttg gtg att ca
                                                                      . 433
Gly Arg Glu Gly Gly Lys Glu Arg Tyr Leu Leu Val Ile
                        10
<210> 145
<211> 200
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<222> 15..200
<221> sig_peptide
<222> 15..92
<223> Von Heijne matrix
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      seq RVCLLSLSLFLWA/NR
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aatacgccag gaac atg cta agg acc tgg agc tct cta ccc tgg acc cgt
                                                                       50
                Met Leu Arg Thr Trp Ser Ser Leu Pro Trp Thr Arg
                                        -20
ttt egg gtt tge ttg etc tet etc tet etc ttt etc tgg get aat egt
                                                                       98
Phe Arg Val Cys Leu Leu Ser Leu Ser Leu Phe Leu Trp Ala Asn Arg
                -10
                                    -5
tta gag gac agt ege tee tge caa eet aat eee atg age etg aet aee
                                                                      146
Leu Glu Asp Ser Arg Ser Cys Gln Pro Asn Pro Met Ser Leu Thr Thr
                            10
                                                 15
ttg ccg ggc cac agg ctc aaa gaa gca gtg tgg ctg cca gca ccc tca
                                                                      194
Leu Pro Gly His Arg Leu Lys Glu Ala Val Trp Leu Pro Ala Pro Ser
    20
                        25
                                             30
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ctt ggg Leu Gly

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<210> 146
<211> 297
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<222> 80..166
<223> Von Heijne matrix
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      seg LVVXWLLPXQCSC/ER
<400> 146
aacaccccag cccaagttca tccccggtcc cttggcagca gtgcgcatcc acaaagccag
cggcacaatt taattactg atg gcc cct ttc cta cga cag gtg gat rtg tgg
                                                                      112
                     Met Ala Pro Phe Leu Arg Gln Val Asp Xaa Trp
                                     -25
gga gca cag gcc ggt ctg gtg gtb gsm tgg tta cta cca tgs caa tgc
                                                                      160
Gly Ala Gln Ala Gly Leu Val Val Xaa Trp Leu Leu Pro Xaa Gln Cys
            -15
                                -10
age tgt gaa ega tea gag eaa tat etg age ace tgt ete eea eag eae
                                                                      208
Ser Cys Glu Arg Ser Glu Gln Tyr Leu Ser Thr Cys Leu Pro Gln His
                                             10
tca agc atc aag cag tcg tgc atc aag cat cca gca ggc ccg atc ccc
                                                                      256
Ser Ser Ile Lys Gln Ser Cys Ile Lys His Pro Ala Gly Pro Ile Pro
                    20
                                         25
gca ggc cac cta cag gga aag gcc aca gct gcg ccc ctg gg
                                                                      297
Ala Gly His Leu Gln Gly Lys Ala Thr Ala Ala Pro Leu
                35
                                    40
<210> 147
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<212> DNA
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<221> sig_peptide
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<223> Von Heijne matrix
      score 7.90000009536743
      seq WLFLVAILKGVRC/EV
<400> 147
agetetgaga gaggageeca geeetgggat etteaggtgt titteactegg tgateaggae
                                                                       60
tgcacagaga gaactcacc atg gag ttt ggg ctg aag tgg ctt ttt ctt gtg
                                                                       112
                     Met Glu Phe Gly Leu Lys Trp Leu Phe Leu Val
                                      -15
gca att tta aaa ggt gtc cgg tgt gaa gtg aag ctg gtg gag tct ggg
                                                                       160
Ala Ile Leu Lys Gly Val Arg Cys Glu Val Lys Leu Val Glu Ser Gly
            -5
gga ggc ctg gtg cag ccg ggg ggg tcc ctg aga ctc tcc tgt gta gga
                                                                       208
Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Val Gly
                        15
                                             20
tet gga tte gte tte gat aaa tat gge ata agt tgg gtg ege cag gea
                                                                      256
Ser Gly Phe Val Phe Asp Lys Tyr Gly Ile Ser Trp Val Arg Gln Ala
25
                    30
                                         35
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cca gga aag ggc cta cag tgg gtc gcg ggg atc ggt ggc ggg gg 300 Pro Gly Lys Gly Leu Gln Trp Val Ala Gly Ile Gly Gly <210> 148 <211> 405 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 21..404 <221> sig_peptide <222> 21..68 <223> Von Heijne matrix score 7.90000009536743 seq AMLVLVVSPWSAA/RG <400> 148 qcqqtcttcc agcagggaaa atg gcg ctg gcc atg ctg gtc ttg gtg gtt tcg 5,3 Met Ala Leu Ala Met Leu Val Leu Val Val Ser -15 ccq tgg tct gcg gcc cgg gga gtg ctt cga aac tac tgg gag cga ctg 101 Pro Trp Ser Ala Ala Arg Gly Val Leu Arg Asn Tyr Trp Glu Arg Leu -5 5 cta cgg aag ctt ccg cag agc cgg ccg ggc ttt ccc agt cct ccg tgg 149 Leu Arg Lys Leu Pro Gln Ser Arg Pro Gly Phe Pro Ser Pro Pro Trp 20 qqa cca qca tta gca gta cag ggc cca gcc atg ttt aca gag cca gca 197 Gly Pro Ala Leu Ala Val Gln Gly Pro Ala Met Phe Thr Glu Pro Ala 35 aat gat acc agt gga agt aaa gag aat tcc agc ctt ttg gac agt atc 245 Asn Asp Thr Ser Gly Ser Lys Glu Asn Ser Ser Leu Leu Asp Ser Ile 50 55 ttt tgg atg gca gct ccc aaa aat aga cgc acc att gaa gtt aac cgg 293 Phe Trp Met Ala Ala Pro Lys Asn Arg Arg Thr Ile Glu Val Asn Arg 65 70 tgt agg aga aga aat ccg cag aag ctt att aaa gtt aag aac aac ata 341 Cys Arg Arg Arg Asn Pro Gln Lys Leu Ile Lys Val Lys Asn Asn Ile 80 85 qac qtt tgt cct gaa tgt ggt cac ctg aaa cag aaa srt gtc ctt tgt 389 Asp Val Cys Pro Glu Cys Gly His Leu Lys Gln Lys Xaa Val Leu Cys 405 gct act gct atg aaa a Ala Thr Ala Met Lys 110 <210> 149 <211> 146 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 56..145 <221> sig_peptide

<222> 56..115 <223> Von Heijne matrix score 7.80000019073486 seq LLLFPLSLLFTLG/FL

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 ttt ttc tac tca cac ttt tta ctt ctt ttt ccc ctc tcg tta ctt ttc
                                                                     106
 Phe Phe Tyr Ser His Phe Leu Leu Phe Pro Leu Ser Leu Leu Phe
                -15
                                    -10
 146
 Thr Leu Gly Phe Leu Phe Val Phe Phe Phe Phe Phe
 <210> 150
 <211> 408
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 <222> 105..407
 <221> sig_peptide
 <222> 105..242
 <223> Von Heijne matrix
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      seq LVLLGTRVPLSGG/GP
 <400> 150
 aaacagggcc attggcaaag ctggggtacc agtcacccag ccacgctcta gggtggtagc
                                                                     60
caagaagacg gaccccgagt gggaggcaga gagacaagag gtgg atg aag cag agc
                                                                    116.
                                                 Met Lys Gln Ser
 aag cgt gas atg gtg aag aga aga cgg agc ccc gcg ctg gga gag gaa
                                                                    164
Lys Arg Xaa Met Val Lys Arg Arg Ser Pro Ala Leu Gly Glu Glu
        -40
                           -35
                                                -30
 cgc ttc agt ccg agt tcc att ctg cac cca agg ctc ccc ttg gtc ctc
                                                                    212
Arg Phe Ser Pro Ser Ser Ile Leu His Pro Arg Leu Pro Leu Val Leu
                        -20
                                            -15
 ctg gga acc agg gtg ccc ctt agt ggt ggc cca gga gaa ccc gac
                                                                    260 .
Leu Gly Thr Arg Val Pro Leu Ser Gly Gly Gly Pro Gly Glu Pro Asp
 -10
                    -5
caa ggc agg agc gcc ccc tcc tgg aag agc ctc gct tca acg cat mat
                                                                    308
Gln Gly Arg Ser Ala Pro Ser Trp Lys Ser Leu Ala Ser Thr His Xaa
                               15
 cat tee egg eeg gea gea geg geg aeg eea gea agg eet geg aet eag
                                                                    356
. His Ser Arg Pro Ala Ala Gly Ala Thr Pro Ala Arg Pro Ala Thr Gln
                           30
                                              . 35
 age cag ett gge ceg tte gee ceg eee ett eee ggt gte ege eee gee
 Ser Gln Leu Gly Pro Phe Ala Pro Pro Leu Pro Gly Val Arg Pro Ala
    40
                        45
 cca t
                                                                    408
 Pro
 55
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cacattttct acttaaaagc aamgttacaa agcctgtgga attgctctga cttagaaaga
acttgatc atg ctt ttg gag tct cta tgt gtt ctc tct ctg ttg gtt agt

Met Leu Leu Glu Ser Leu Cys Val Leu Ser Leu Leu Val Ser

-15

-10

-5

ttt aaa tca gcc tgc ctc aca agg gag cct gca ttt gat tcc caa gcc

Pho Lys Ser Ala Cys Leu Thr Arg Glu Pro Ala Phe Asp Ser Gln Ala

Phe Lys Ser Ala Cys Leu Thr Arg Glu Pro Ala Phe Asp Ser Gln Ala

1 5 10

cgc ccg gg · 166
Arg Pro

<210> 152

<211> 382

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<222> 99..380

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<222> 99..236

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-45

260

aag cag ccg ctg att acc ctt gca aag aaa tct gta aaa tgt gca cgt
Lys Gln Pro Leu Ile Thr Leu Ala Lys Lys Ser Val Lys Cys Ala Arg
-40 -35 -30 -25
gaa tgt ctg aga tgc tct ctc agg cct cta gtc ctt ctg tat ctt tcc 212

Glu Cys Leu Arg Cys Ser Leu Arg Pro Leu Val Leu Leu Tyr Leu Ser
-20 -15 -10

ttt gca gcc ctg ggt gta gta gca ctc agg agt gtt gaa tca ccc ctg Phe Ala Ala Leu Gly Val Val Ala Leu Arg Ser Val Glu Ser Pro Leu

gcc gag acc cac tcc tgc tgg ctc agc ctg ggc atg tgt gtg ctc cag 308
Ala Glu Thr His Ser Cys Trp Leu Ser Leu Gly Met Cys Val Leu Gln

10 15 20

tgt gaa cag cag tgg gtt cca acc cca gtc tcc ttt ctc tgt ggc ctc

Cys Glu Gln Gln Trp Val Pro Thr Pro Val Ser Phe Leu Cys Gly Leu

25 30 35 40

tct ggc tcc agc acc atc atc gtt ag

Ser Gly Ser Ser Thr Ile Ile Val

382

4

<210> 153

<211> 208

<212> DNA

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<222> 10..207

kazar sig_peptide
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seq Cvivvehvacvhe/vv
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Met Cys Val Val Cys Ser Val His Gly Val Cys Cys Val Tyr -20 -15
gtg gtg tgc ctg gtg tcg tgt gtt ttg tgt gtc gtg tgt cct gtg tgt
Val Val Cys Leu Val Ser Cys Val Leu Cys Val Val Cys Pro Val Cys -10 -5 1 5
tgg gtt atg tgt tgt gtg tgg tgc atc tgt gtg tgt gtg tgg tgt gtc 147
Trp Val Met Cys Cys Val Trp Cys Ile Cys Val Cys Val Trp Cys Val 10 15 20
tgt tgt atg tgt tgt gtg ttg tca tgt gtt gtg tca cat ggg ttg tgt 195
Cys Cys Met Cys Cys Val Leu Ser Cys Val Val Ser His Gly Leu Cys 25 30 35
ggt gtg tca tgg g 208
Gly Val Ser Trp 40
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<222> 73249
221) signestide
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score 7.80000019073486
seq WVFLVAVLEVVQC/EI
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agaggactca cc atg gaa ctg ggg ctg tcc tgg gtc ttc ctt gtt gct gtt 111
Met Glu Leu Gly Leu Ser Trp Val Phe Leu Val Ala Val
-15 -10
tta gaa gtt gtc cag tgt gaa att caa ctg att gac gcc ggg gga ggc 159 Leu Glu Val Val Gln Cys Glu Ile Gln Leu Ile Asp Ala Gly Gly
-5 1 5 10
cac gtc cag gcg ggg ggg tca ctg aga ctc tcc tgt gtt gcc tct gac 207
His Val Gln Ala Gly Gly Ser Leu Arg Leu Ser Cys Val Ala Ser Asp 15 20 25
ttc ctg ttt aga agc tat tgg atg acc tgg gtc cgc cat ccg gg 251
Phe Leu Phe Arg Ser Tyr Trp Met Thr Trp Val Arg His Pro 30 35 40
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<222> 24..140
<223> Von Heijne matrix
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      seq ILLFLFLILFIWH/IR
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                          Met Ser Ile Leu Leu Arg Val Leu Gly Ile
                                          .-35
aag gga tgc tgg att ttg tca aat cct ttt tct gca tgt att gag atg
                                                                      101
Lys Gly Cys Trp Ile Leu Ser Asn Pro Phe Ser Ala Cys Ile Glu Met
                -25
                                    -20
                                                                      147
atc ttq tta ttt ttg ttt tta att ctg ttt ata tgg cac att cgg g
Ile Leu Leu Phe Leu Phe Leu Ile Leu Phe Ile Trp His Ile Arg
<210> 156
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atg gct gaa aaa gcg ggg tct aca ttt tca cac ctt ctg gtt cct att
                                                                       108
Met Ala Glu Lys Ala Gly Ser Thr Phe Ser His Leu Leu Val Pro Ile
                    -20
-25
                                                                       141
ctt ctc ctq att ggc tgg att gtg ggc tgc acc
Leu Leu Leu Ile Gly Trp Ile Val Gly Cys Thr
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             Met Ala Glu Ser Arg Gly Arg Leu Tyr Leu Trp Met Cys
                              -15
ttg gct gct gcg ctg gca tct ttc ctg atg gga ttt atg gtg ggc tgg
                                                                        98
Leu Ala Ala Ala Leu Ala Ser Phe Leu Met Gly Phe Met Val Gly Trp
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WO 99/53051 PCT/IB99/00712 96 ttt att aag cct ctg gg 115 Phe Ile Lys Pro Leu <210> 158 <211> 175 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 54..173 <221> sig_peptide <222> 54..131 <223> Von Heijne matrix score 7.69999980926514 seq FLLLLYFFXIAVT/HP <400> 158 caattcaaca tgagatttag tggtgacaaa tatccaaact ctatcaacct cta atg 56 etg ace tea etg cet tte etc etg ecc ace ate age ttt etc etc etc 104 Leu Thr Ser Leu Pro Phe Leu Leu Pro Thr Ile Ser Phe Leu Leu -20 -15 ttg tat ttt ttt cma att gct gtc acc cat ccg tca gtt ctc atc aac 152

Leu Tyr Phe Phe Xaa Ile Ala Val Thr His Pro Ser Val Leu Ile Asn -5 ttc tct ttc tcc ttc ccc aga tc 175 Phe Ser Phe Ser Phe Pro Arg 10

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<210> 160 <211> 346 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 202..345 <221> sig peptide <222> 202..282 <223> Von Heijne matrix score 7.59999990463257 seq WTLLSISLSVFWS/EP <400> 160 ttcttctaca tacagctacc caactagccc acaccattta ttgaatacag agtagtcttt tccctgttgg ttatttttct taactttgtt aaagatcaga tatctgtagg tgtgcagctt 120 tatttctggg ttttctgttc cgttccattg gtctatgtgt ctgtttttgt accagtacca 180 tgctgttctg gcaccagtac c atg cta ttt tgg tta cca tct cca tct gag 231 Met Leu Phe Trp Leu Pro Ser Pro Ser Glu -25 -20 acc act tca gcc tgg act tta ttg tcc ata tca cta tca gta ttt tgg 279 Thr Thr Ser Ala Trp Thr Leu Leu Ser Ile Ser Leu Ser Val Phe Trp -10 tca gag cca ttc aat aag tct cta gga agt tcc aaa cta cca tgt cat 327 Ser Glu Pro Phe Asn Lys Ser Leu Gly Ser Ser Lys Leu Pro Cys His ttt ttt tct ata aaa cgg g 346 Phe Phe Ser Ile Lys Arg <210> 161 <211> 388 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 194..388 <221> sig_peptide <222> 194..334 <223> Von Heijne matrix score 7.59999990463257 seq LXLGEGLTFLCLC/QV <221> misc feature <222> 352 <223> n=a, g, c or t <400> 161 agtgagagct tagtcttggt actatttgtt tttgtttctt actgtttgtc tgtttatggt 120 tggttgcaag aaaattgtgt tgtaaattat cccttgcttt ctctattagt taatagcctt ccccttctgt agtaaagtaa msagsctttt kcctgttcaa atattttagg cttgttttt 180 gttttgattg tac atg cct gtg tgt ttt tat tcc tta att tgt ttc ttt 229 Met Pro Val Cys Phe Tyr Ser Leu Ile Cys Phe Phe -45 -40 att tat ttc tgt ttg tta tct cca aga gaa aca ata gaa gag gtg gcc 277 Ile Tyr Phe Cys Leu Leu Ser Pro Arg Glu Thr Ile Glu Glu Val Ala

WO 99/53051 PCT/IB99/00712 98 -30 -35 -25 ctc ttc cag ttt tct ctg cth mtc ttg gga gag ggt ctc acc ttt ctt 325 Leu Phe Gln Phe Ser Leu Leu Xaa Leu Gly Glu Gly Leu Thr Phe Leu -15 -10 tgc ctc tgc cag gta atg acg aat aan atg caa ctg ctg ttc ttg agt 373 Cys Leu Cys Gln Val Met Thr Asn Xaa Met Gln Leu Leu Phe Leu Ser ggg gta gtc tgt ggg 388 Gly Val Val Cys Gly . 15 <210> 162 <211> 235 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 172..234 <221> sig peptide <222> 172..210 <223> Von Heijne matrix score 7.5 seq MAPLLLSLSCSFS/CH cccctccaaa tctcatgttg agatttgatc cctaatgttg gagatggggc ctggtgggag 60 atatteggat catgagggca gateceteae taatggcetg gtgcceteee tgtggaaatg 120 agtaagttct cactcttttg gttcacctga gagctgtttg tttaaaagag c atg gca 177 ecc etc ett etc tet etg tet tge tec ttt tet tge eat gtg aca etc 225 Pro Leu Leu Ser Leu Ser Cys Ser Phe Ser Cys His Val Thr Leu -10 -5 ctg ccc cgg g 235 Leu Pro Arg <210> 163 <211> 240 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 99..239 <221> sig_peptide <222> 99..158 <223> Von Heijne matrix score 7.5 seq LLWVLLLNLGPRA/AG <400> 163 aaaacgaccc ggtgggtcta cagcggaagg gagggagcga aggtaggagg cagggcttgc 60 etcactggcc acceteccaa ecceaagage ceageece atg gte eee gee gee ggs 116 Met Val Pro Ala Ala Gly -20 geg etg etg tgg gte etg etg etg aat etg ggt eee egg geg geg ggg 164

Ala Leu Leu Trp Val Leu Leu Leu Asn Leu Gly Pro Arg Ala Ala Gly

gcc caa ggc ctg acc cag act ccg acc gaa atg cag cgg gtc agt tta

Ala Gln Gly Leu Thr Gln Thr Pro Thr Glu Met Gln Arg Val Ser Leu

-5

-25

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                     Met Val Phe Trp Glu Ile Ser Val Gln Ile Ile
                                      -20
ctg atc tct gaa ctc ctg ctg ttg agg tca gtc act tca cac aat acc
                                                                      100
Leu Ile Ser Glu Leu Leu Leu Arg Ser Val Thr Ser His Asn Thr
            -10 .
                              - -5
atg atg aga gct tta tca agc cag atg ctt agt cag agc ttt cca aga
                                                                      148
Met Met Arg Ala Leu Ser Ser Gln Met Leu Ser Gln Ser Phe Pro Arg
                        10
                                            15 .
ccc age ttt ggt ttt atc age aaa atc cat cct tcc cac ccc ccc aa
                                                                      195
Pro Ser Phe Gly Phe Ile Ser Lys Ile His Pro Ser His Pro Pro
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                                      Met Phe Phe Leu Asn Ile Ala
                                          -50
atg ttc att gtg gta atg gtg cag atc tgt ggg agg aat ggc aag aga
                                                                      102
Met Phe Ile Val Val Met Val Gln Ile Cys Gly Arg Asn Gly Lys Arg
                -40
                                     -35
age aac egg acc etg aga gaa gtg tta agg aac etg egc agt gtg
                                                                      150
Ser Asn Arg Thr Leu Arg Glu Glu Val Leu Arg Asn Leu Arg Ser Val
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-20

-15

WO 99/53051 PCT/IB99/00712 100 gtt agc ttg acc ttt ctg ttg ggc atg aca tgg ggt ttt gca ttc ttt 198 Val Ser Leu Thr Phe Leu Leu Gly Met Thr Trp Gly Phe Ala Phe Phe -5 gcc tgg gga ccc tta aat atc ccc ttc atg tac ctc ttc tcc atc ttc 246 Ala Trp Gly Pro Leu Asn Ile Pro Phe Met Tyr Leu Phe Ser Ile Phe 15 aat tca tta c 256 Asn Ser Leu <210> 166 <211> 209 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 36..209 <221> sig_peptide <222> 36..86 <223> Von Heijne matrix score 7.5 seq FLFLFLLXXLIVA/VT <400> 166 cttttttdtc ckgcacaagg gatttccggg tcagg atg aac aaa cac ttc ttg 53 Met Asn Lys His Phe Leu -15 ttc ctc ttc ctc ctt dac kgc ctc att gtg gca gtg aca tca ctt cag 101 Phe Leu Phe Leu Leu Xaa Xaa Leu Ile Val Ala Val Thr Ser Leu Gln tgc ata aca tgc cac ctt cgc aca cgg aca gac cgc tgt aga aga ggc 149 Cys Ile Thr Cys His Leu Arg Thr Arg Thr Asp Arg Cys Arg Arg Gly 15 ttt ggt gdc tgt act gct cag aag ggc gag gca tgc atg ctc tta agg 197 Phe Gly Xaa Cys Thr Ala Gln Lys Gly Glu Ala Cys Met Leu Leu Arg 30 209 att cac cag cgc Ile His Gln Arg 40 <210> 167 <211> 184 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 44..184 <221> sig_peptide <222> 44..148 <223> Von Heijne matrix score 7.5 seg LLLTSHFLGESLG/GG <400> 167 taaagtootg tgtatgacat gacatagtat ttgogtaatt taa atg tac ata aag 55 Met Tyr Ile Lys -35 atg gag tot gte ace ttg tea eea gee eea gte tte eee gte eet gea 103

Met Glu Ser Val Thr Leu Ser Pro Ala Pro Val Phe Pro Val Pro Ala

-25

-30

101	
car ctc ctt tta ctg aca tcc cat ttt cta ggc gag tcc ctt ggt gga Gln Leu Leu Leu Thr Ser His Phe Leu Gly Glu Ser Leu Gly Gly -15 -10 -5 1	151
ggc aca ctg ctt gtc cca ctc ctc ccc cca ggg Gly Thr Leu Leu Val Pro Leu Leu Pro Pro Gly 5 10	184
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gggacagcaa gacctccgct caggcccctc tttcga atg ckc cam gcm ctc ctg Met Xaa Xaa Ala Leu Leu -25	114
cga tot aga atg att cag ggc agg atc ctg ctc ctg acc atc tgc gct Arg Ser Arg Met Ile Gln Gly Arg Ile Leu Leu Leu Thr Ile Cys Ala -20 -15 -10	162
gcc ggc att rgt ggg act cgt cag ttt ggc tat aac ctc tct atc atc Ala Gly Ile Xaa Gly Thr Arg Gln Phe Gly Tyr Asn Leu Ser Ile Ile -5 1 5 10	210
aat gac cc	218
Asn Asp	
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cggcgyrrgt gmtgtccagc ttcccggtgc tgaaaaccgg agggctcgtc atccaccact	120
accatgtaag ggccatgaga agggctcatc ctggcgcasg cggacatgga ggaggactta	180
ttccagctaa ggcagctgcc ggttgtgaaa ttccgtcgca caggcgagag tgcaaggtca gaggacgaca cggcttcagg agagcatgaa gtccagattg aaggggtcca cgtgqqccta	240 300
gaggctgtgg agctgg atg atg ggg cak ctg tgc cca agg agt ttg cca atc Met Met Gly Xaa Leu Cys Pro Arg Ser Leu Pro Ile -45	352
cca ccg atg ata ctt tca tgg tgg aag atg cag tgg aag cca ttg gct	400
Pro Pro Met Ile Leu Ser Trp Trp Lys Met Gln Trp Lys Pro Leu Ala -35 -25 -20	

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102
ttg gaa aat ttc agt gga agc tgt ctg ttc tca mtg gct tgg ctt kga
Leu Glu Asn Phe Ser Gly Ser Cys Leu Phe Ser Xaa Ala Trp Leu Xaa
                -15
                                     -10
tgc tsa tgc cat gga gat gat gat ctc agc at
                                                                       480
Cys Xaa Cys His Gly Asp Asp Leu Ser
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gggaagaaag ggcaggcggc tcggcgggcg tcttctccac tccntgccgc gccccgtggc
                                                                      120
tgcagggagc cggc atg ggg ctt ctc cag ttg cta gct ttc agt ttc tta
                                                                      170
                Met Gly Leu Leu Gln Leu Leu Ala Phe Ser Phe Leu
                                     -10
ggt aat tcc gtg gaa acg gtg cgg gga ggc gga cgg act tgg gca tgg
                                                                      218
Gly Asn Ser Val Glu Thr Val Arg Gly Gly Gly Arg Thr Trp Ala Trp
gga agg aaa acc caa aag ctg ctt gct cac ctt cgt ggg atc ctg ggg
                                                                      266
Gly Arg Lys Thr Gln Lys Leu Leu Ala His Leu Arg Gly Ile Leu Gly
gct tgg gas agg ga
                                                                      280
Ala Trp Xaa Arg
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                              Met Leu Val Leu Val His Ser Ser Leu
                                               -10
age aag ace ttg tet cag aaa aaa aaa aag tte aca aas ccc ace agg g
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                                                                       60
tttgatgtet et atg tee tte agt tet get etg att tta gtt att tet tge
                                                                      111
              Met Ser Phe Ser Ser Ala Leu Ile Leu Val Ile Ser Cys
                              -15
ctt ctg cta gct ttt gaa tgt gtt tgc tct tgc ttt tct ggt tct ttt
                                                                      159
Leu Leu Leu Ala Phe Glu Cys Val Cys Ser Cys Phe Ser Gly Ser Phe
                        1
aat tgt gat gtt agg gtg tca att tcg gat ctt tcc tgc ttt ctc ttg
                                                                      207
Asn Cys Asp Val Arg Val Ser Ile Ser Asp Leu Ser Cys Phe Leu Leu
                                    20
tgg ggc aag gg
                                                                      218
Trp Gly Lys
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                                                                       60
ctttggtttg aatttcctcc tgtagcttgg agtagtttga tcatctgaag ctttcttctc
                                                                      120
tcaactcatc aaagtcattc tccatccagc tttgttccat tgctggtgag gaactgtgtt
                                                                      180
ccttcggagg aggagaggtg ctctgctttt ttgagtttcc agtttttctg ctctgtttt
                                                                      240
tececatett tgtggtttta tetaettttg gtetttgatg etggtgatgt acag atg
                                                                      297
ggt ttt tgg tgt gga tgt cct ttc tgt ttg twa gtt ttc ctt cta aca
                                                                      345
Gly Phe Trp Cys Gly Cys Pro Phe Cys Leu Xaa Val Phe Leu Leu Thr
    -20
                        -15
gac agg acc ctc agc tgc agg tct gtt gga gtt gc
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Asp Arg Thr Leu Ser Cys Arg Ser Val Gly Val
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	aa gtg ln Val														1	101
tct to Ser Se	ec tcc er Ser 5	cca Pro	tca Ser	999 Gly	gca Ala	gtg Val 10	ccc Pro	acg Thr	tct Ser	ttg Leu	gag Glu 15	ctg Leu	cag Gln	cga Arg	. 1	149
	eg gat nr Asp														, 1	197
	eg gcc co Ala						g								2	222
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	et tgg er Trp								999					gag	1	101
	cg ccg ro Pro 5														j	149
	gg gat rg Asp)					g										171
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PCT/IB99/00712

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ttgattgcat ggtcagagtg aatctgtgct gtacccawat tcagtagcct tctcctatcc
                                                                   120
179
aat gga att ttc ttg ctc ttg atc tct gtc tta aca gtg att tgg ttt
                                                                   227
Asn Gly Ile Phe Leu Leu Leu Ile Ser Val Leu Thr Val Ile Trp Phe
   -15
                       -10
                                           -5
tgg aag aca cac ccg ggg
                                                                   245
Trp Lys Thr His Pro Gly
<210> 181
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     score 7.19999980926514
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aaacaaggga tttcgttccc ccctcvcctt ttgtgtaggc tggttaataa actctgtgtt
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tywtagcatt gtcgtgaawa ttcagagtgc tccctgcga atg gtt ttc cta gta
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                                         Met Val Phe Leu Val
ket etg ttg tgt ate att ket ett tat ttg att egt ggt tet gag tgg
                                                                   222
Xaa Leu Leu Cys Ile Ile Xaa Leu Tyr Leu Ile Arg Gly Ser Glu Trp
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gct ttg ttc ttt ttg ctt agg att gct ttg gct agt tgg gct ctc ttt Ala Leu Phe Phe Leu Leu Arg Ile Ala Leu Ala Ser Trp Ala Leu Phe -10 -5 1	162									
tgg atc cat atg aat ttt aga aga gct ttt ttc cac tta cgg tgg ttt Trp Ile His Met Asn Phe Arg Arg Ala Phe Phe His Leu Arg Trp Phe 5 10 15	210									
gat atc aat agc act gaa tct gta aat tgc ttt ggg cag tat ggc cta Asp Ile Asn Ser Thr Glu Ser Val Asn Cys Phe Gly Gln Tyr Gly Leu 20 25 30	258									
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tct tta tta gtt ttc tgc ctc aat gat ctw tck aat gcw gtc arg wgg Ser Leu Leu Val Phe Cys Leu Asn Asp Leu Ser Asn Ala Val Xaa Xaa -10 -5 1	155									
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cagcatcgga ggtgcctcag cc atg gca tgg atc cct ctc ttc ctc ggc gtc	60 112									
Met Ala Trp Ile Pro Leu Phe Leu Gly Val										

-15 ctt gct tac tgc aca gga tcc gtg gcc tcc tat gag ctg act cac cca 160 Leu Ala Tyr Cys Thr Gly Ser Val Ala Ser Tyr Glu Leu Thr His Pro -5 1 ccc tca qtg tcc gtg tcc cca gga cag aca qcc aqc atc acc tqc tct 208 Pro Ser Val Ser Val Ser Pro Gly Gln Thr Ala Ser Ile Thr Cys Ser 20 gga gat aaa ttg ggg gat aaa tat gct tgc tgg tat cag cag aag cca 256 Gly Asp Lys Leu Gly Asp Lys Tyr Ala Cys Trp Tyr Gln Gln Lys Pro ggc cag tcc cct gtg ctg gtc atc tat caa gat agc aag cgg ccc tca 304 Gly Gln Ser Pro Val Leu Val Ile Tyr Gln Asp Ser Lys Arg Pro Ser 50 ggg atc cct gag cga ttc tct ggc tcc aac tct ggg aac aca gcc act 352 Gly Ile Pro Glu Arg Phe Ser Gly Ser Asn Ser Gly Asn Thr Ala Thr 65 70 ctg acc atc agc ggg acc cag gct atg gat gag gct gac tat tac tgt 400 Leu Thr Ile Ser Gly Thr Gln Ala Met Asp Glu Ala Asp Tyr Tyr Cys 80 85 90 cag gcg tgg gac agc agc act gtg gta ttc ggc gga ggg acc a 443 Gln Ala Trp Asp Ser Ser Thr Val Val Phe Gly Gly Gly Thr <210> 185 <211> 427 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 332..427 <221> sig peptide <222> 332..418 <223> Von Heijne matrix score 7.09999990463257 seq FCFXLCFGRSSLC/CR <400> 185 taagtttata yhtotgaato tgaaatcaga atatatatat ttaattttto aattttaaaa 60 atgttaccct gtgtgagaca aaacaaaaca gtgactagaa ccctccttgt gggctaaatt 120 tgagtttgct tcttcataat gttttaaatg cttcacaaac atttttcttt ggtatattga 180 gcaaaatgaa ttgaagtata tttactgagt gatgattatt gaggaaaaac tcaaagatct 240 gctgtaagca ctagagttga aggactagcc caacagctcc tcaggcacct ttgggtatat 300 tgagttgccc cccctgactt tgaacacatc t atg gtc tgt gtc atc ttc aaa 352 Met Val Cys Val Ile Phe Lys gag etc atg gaa ttt gaa ttc ect ggg ttt tgt ttt tgh ett tgt ttt 400 Glu Leu Met Glu Phe Glu Phe Pro Gly Phe Cys Phe Xaa Leu Cys Phe -15 gga cgg agc tcg ctc tgt tgc cga rac 427 Gly Arg Ser Ser Leu Cys Cys Arg Xaa -5 <210> 186 <211> 365 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 130..363

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Arg

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                                                                      105
Ile Leu Tyr Leu Phe Phe Leu Lys Trp Ser His Pro Gly Trp Ser
    -15
                        -10
                                            -5
gca acg ncg tgg tct tgg cac act gca acc tcc gcc tcc ctg att caa
                                                                      153
Ala Thr Xaa Trp Ser Trp His Thr Ala Thr Ser Ala Ser Leu Ile Gln
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gtg att ctc ccg cct tgg g
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Val Ile Leu Pro Pro Trp
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                                                   Met Thr Pro
tgt ttt ctg caa atg gac aat ttg act cct ctt ttc cta tct gga tgc
                                                                      103
Cys Phe Leu Gln Met Asp Asn Leu Thr Pro Leu Phe Leu Ser Gly Cys
            -20
                                -15
ttt tta ttt ctc tct cwt tgc wtg att tat ttg gct agg att ttg gg
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                                                                       120
agaagcccgg cgacggagga acgcaggtct gctgccaggg attgaggaga ctgaagaacg
                                                                       180.
ctgaagacag gctg atg ggc tca gct ggt agg ctc cac tat ctc gsc atg
                                                                       230
                Met Gly Ser Ala Gly Arg Leu His Tyr Leu Xaa Met
act get gaa aat eee act eet gga gae etg get eeg kee eee etc ate
                                                                       278 . -
Thr Ala Glu Asn Pro Thr Pro Gly Asp Leu Ala Pro Xaa Pro Leu Ile
            -25
                                 -20
act tgc aaa ctc tgc ctg tgt gag cag tct crt gga caa gat gac cac
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Thr Cys Lys Leu Cys Leu Cys Glu Gln Ser Xaa Gly Gln Asp Asp His
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act cca gga atg c
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Thr Pro Gly Met
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                                                                       113
                                       Met Asn His Leu Pro Pro
aac cat tat agg mgc cat gtg ttc aca tgt cat gtg gac cag tat tta
                                                                       161
Asn His Tyr Arg Xaa His Val Phe Thr Cys His Val Asp Gln Tyr Leu
            -40
                                 -35
act gtg gaa acc gcg ggt ggc atg gag aag gag gca gtg tcc gtg act
                                                                       209
Thr Val Glu Thr Ala Gly Gly Met Glu Lys Glu Ala Val Ser Val Thr
                            -20
                                                 -15
gtg ctg ctc tcc gca gcc ccc tgc ctg ctg tcc tgt ttc ctc ggc tcc
                                                                       257
Val Leu Leu Ser Ala Ala Pro Cys Leu Leu Ser Cys Phe Leu Gly Ser
                        -5
teg gtg tet gga etg geg tte tgg gtt tee cag cag aaa aet aaa ggg
                                                                       305
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Ser Val Ser Gly Leu Ala Phe Trp Val Ser Gln Gln Lys Thr Lys Gly 10 15 20	
cca gag agg tgt aaa aac aca cac cac tbg gca gnt aat aat ttc ccc	353
Pro Glu Arg Cys Lys Asn Thr His His Xaa Ala Xaa Asn Asn Phe Pro	
gcg agg	359
Ala Arg	202
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Met Asn Lys Ile Lys Glu Asn Thr His Thr His	170
-40 -35 -30	
aca cac aca cac aca cac aaa aac aac acc aaa cta gtg tca aac cta	218
Thr His Thr His Lys Asn Asn Thr Lys Leu Val Ser Asn Leu	
-25 -20 -15	
ttc ctt ttt atg tta cct ctc tgg tgc tcc att ggc act tgc aca g	264
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score 7 seq LFLYSLFTENVLA/HP <400> 193	60
score 7 seq LFLYSLFTENVLA/HP	60 120
score 7 seq LFLYSLFTENVLA/HP <400> 193 tgtattgttt mmmttattta ctagtatgca gatctggttt tcattcttt catattgaat	
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114

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Met Asn Leu Gly Gly His Ser Asp His Ser Thr Phe Leu Phe Phe Leu
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                            -15
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Ala Ile Phe Ala Val Thr Phe Leu Leu Ala Leu Val Gly Ala Val Leu
                            -10
tac ctc tat ccg gct tcc aga caa gct gca gga att cca ggg att act
                                                                      153
Tyr Leu Tyr Pro Ala Ser Arg Gln Ala Ala Gly Ile Pro Gly Ile Thr
    1
                                        10
cca act gaa gaa aaa gat ggt aat ctt cca gat att gtg aat agt gga
                                                                      201
Pro Thr Glu Glu Lys Asp Gly Asn Leu Pro Asp Ile Val Asn Ser Gly
                20
                                    25
agt ttg cat gag tbc ctg gtt aat ttg cat gag aga tat ggg cct gtg
                                                                      249
Ser Leu His Glu Xaa Leu Val Asn Leu His Glu Arg Tyr Gly Pro Val
                                40
gtc tcc ttc tgg ttt ggc agg cgc ctc gtg gtt agt ttg ggc act gtt
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Val Ser Phe Trp Phe Gly Arg Arg Leu Val Val Ser Leu Gly Thr Val
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                                                                      102
Leu Glu Leu Leu Gly Ser Ser Pro Pro Ile Ser Ala Ser Gln Ser
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Thr Gly Ile Thr Ser Val Ser
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                   Met Pro Ser Gln Leu Leu Leu Ser Leu Ser
                           -15
ctc ttt ttq ttt ttt tgg aga cag agt ctc gtt ttg tgg ccc agg ctg
                                                                      158
Leu Phe Leu Phe Phe Trp Arg Gln Ser Leu Val Leu Trp Pro Arg Leu
gag tgc agt tgt gtc att gcg gct cac tgc agc ctg acc tcc cag gct
                                                                      206
Glu Cys Ser Cys Val Ile Ala Ala His Cys Ser Leu Thr Ser Gln Ala
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cgg g
Arg
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cagtataaaa tatataatat acactaat atg tat act aat aaa tat aca cta
                                                                      112
                               Met Tyr Thr Asn Lys Tyr Thr Leu
                                   -45
ata tat aac ata cta ata tat aat ata tgt btk drg tat atg tgg ttg
                                                                      160
Ile Tyr Asn Ile Leu Ile Tyr Asn Ile Cys Xaa Xaa Tyr Met Trp Leu
            -35
                                -30
ata ctc att tat atg tac cta cat att tgc ctc ttt tgt tgc wct ttt
                                                                      208
Ile Leu Ile Tyr Met Tyr Leu His Ile Cys Leu Phe Cys Cys Xaa Phe
                            -15
att tot too tgo aat tot gtg ttt occ tgt gtg att atb ttt ott otg
                                                                      256
Ile Ser Ser Cys Asn Ser Val Phe Pro Cys Val Ile Xaa Phe Leu Leu
cct gaa gaa ctt ctt twt gtd twt ctd wdw dtg tnt tty wtt gtg aga
                                                                      304
Pro Glu Glu Leu Leu Xaa Val Xaa Leu Xaa Xaa Yaa Phe Xaa Val Arg
                                    20
tgg agt ctc amt cwg tcg tcc agg ctg gag tgc a
                                                                      338
Trp Ser Leu Xaa Xaa Ser Ser Arg Leu Glu Cys
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tggcatggga acaagaattt aca atg tta ctc acc cac aat gaa gat tac atg
                                                                      113
                         Met Leu Leu Thr His Asn Glu Asp Tyr Met
                              -30
cct ggc aat ttd grc ttw ard daw ttg tgg agc tta att cag gct gtt
                                                                      161
Pro Gly Asn Xaa Xaa Xaa Xaa Leu Trp Ser Leu Ile Gln Ala Val
    -20
                        -15
cat atc tgc cta ggc agg aaa aaa aaa
                                                                      188
His Ile Cys Leu Gly Arg Lys Lys
-5
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ago rat dyt cot goo toa aco too oga gta gvy ggg att aca ggo atg

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cgc
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Arg
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gtttgtcaga gaaagtcttt atttctcctt catgcttgaa ggatgtttcc accggatata
                                                                       120
ctatcctagg gtaaaagttt ttttccttca gcactttaaa t atg tca tgc cac tct
                                                                       176
                                               Met Ser Cys His Ser
ctt ctg gcc tgt aag gtt ttc act gaa aag tct cct acc aaa cat att
                                                                       224
Leu Leu Ala Cys Lys Val Phe Thr Glu Lys Ser Pro Thr Lys His Ile
            -30
                                -25
aga gag cac cat tgt atg tta ttt gtt tct ttt ctc ttg ctg ctt tta
                                                                       272
Arg Glu His His Cys Met Leu Phe Val Ser Phe Leu Leu Leu Leu Leu
       -15
                            -10
gga tcc cgg gg
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Gly Ser Arg
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                                                                       60
ggagagetgg ggegeeeacg agaggateee teaceegggt eteteeteag gg atg aca
                                                                       118
                                                           Met Thr
tca tcc gtc cac ctc ctt gtc ttc aag gac cac ctc ctc tcc atg ctg
                                                                       166
Ser Ser Val His Leu Leu Val Phe Lys Asp His Leu Leu Ser Met Leu
                -20
                                    -15
age tge tge caa ggg gee tge tge cea tet aca cet cae gag gge act
                                                                       214
Ser Cys Cys Gln Gly Ala Cys Cys Pro Ser Thr Pro His Glu Gly Thr
agg age acg gtt tee tgg ate eea eea ea tae aaa gea gee aca eag
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cacaqatttg tggcttttta tgaaatacac ctgtagatta atttwcagtt thtwhayggw
                                                                       120
agtagacagt caaaggctag atcactgtra tgagtagggc ttccacattt aagaaaaagc
                                                                       180
tqtaatqaag tgaattgaat cttgcttctt ttgggtcacc caaaagcagt gataagtgct
                                                                       240
qaqtqttat ggcacttatt aacaaaagta actcagaatt gctgtctann cctccatatc
                                                                       300
ttttttcttc tctccgtgta gttctaaaaa tgaccatatg atattccttg a atg gta
                                                                       357
aga geg tet att ett ett age atg tte tgt gtg tea eac act gtg eag
                                                                       405
Arg Ala Ser Ile Leu Leu Ser Met Phe Cys Val Ser His Thr Val Gln
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        -15
                                                 -5
aca gca aca tac aca ca
                                                                       422
Thr Ala Thr Tyr Thr
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                                           Met Glu Lys Thr Ala Leu
                                                   -15
tca tcc. ttt acg tgg tgg gca cct gcc tgc tgt gct cca cgt aca tac
                                                                       104
Ser Ser Phe Thr Trp Trp Ala Pro Ala Cys Cys Ala Pro Arg Thr Tyr
    -10
                         -5
gtg gtg tct gca aca act ctg tca gct gtg caa ggt cac tgt cct cta
                                                                       152
Val Val Ser Ala Thr Thr Leu Ser Ala Val Gln Gly His Cys Pro Leu
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PCT/IB99/00712

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ctg gct ctt tct ccg gac cta cag gca gcc aga ggr ctg atg tgt gct

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123
 Leu Ala Leu Ser Pro Asp Leu Gln Ala Ala Arg Gly Leu Met Cys Ala
         -10
                              -5
 gct tcc gtg atg tcc ttc ttg gct ttc atg atg g
                                                                        368
 Ala Ser Val Met Ser Phe Leu Ala Phe Met Met
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                                                                       120
 gggccgtatg gcatttgggc aatattgatt cttcctattc atgagcatgg aatqtttttc
                                                                       180
catttgttca tgtcctctct tattttgttg agcagtggtt tgtagttctc cttgaagggq
                                                                       240
 ttottcacat coottgtaag ttgtattooc aggtatttta ttototttgt agcaattttq
                                                                       300
 aatgggagtt cactc atg att tgg ctc tct ttt tgt cta tta ttg gtg tat
                                                                       351
                  Met Ile Trp Leu Ser Phe Cys Leu Leu Leu Val Tyr
 agg aat get tgt gat ttt tge aca ttg act tta tat eet ggg act ttg
                                                                       399
 Arg Asn Ala Cys Asp Phe Cys Thr Leu Thr Leu Tyr Pro Gly Thr Leu
             -25
                                 -20
 ctg aag ttg ctt atc agc tta agg agt ttt tgg gct gag acg acg ggg g
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 Leu Lys Leu Leu Ile Ser Leu Arg Ser Phe Trp Ala Glu Thr Thr Gly
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                                                                        54
                               Met Phe Ser Ser Pro Gly Leu Arg Thr
                               -25
                                                    -20
 ctc ttt gta ttg gta ggc agc ctg cac ttg ttc ctt tca gtc ctq gca
                                                                       102
 Leu Phe Val Leu Val Gly Ser Leu His Leu Phe Leu Ser Val Leu Ala
                          -10
 agt aaa agc agg aat tot aaa aag caa cga tta tto oto cta gtt cot .
                                                                       150
 Ser Lys Ser Arg Asn Ser Lys Lys Gln Arg Leu Phe Leu Leu Val Pro
                 5
                                     10
 ttg tac ag
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                                        -25
99
Ala Arg Val Arg Pro Leu Phe Cys Ala Leu Leu Leu Ser Leu Xaa Xaa
                -15
                                    -10
mty ckt ccg rkg cka cgs cgt gkg agg aga ccc cgc ggt cgc gtt gcc
                                                                    147
Xaa Xaa Pro Xaa Xaa Arg Arg Xaa Arg Arg Pro Arg Gly Arg Val Ala
                                               10
aca tog cog ttt cga gta saa ata cag ctt caa ggg gcc gca cct ggt
                                                                    195
Thr Ser Pro Phe Arg Val Xaa Ile Gln Leu Gln Gly Ala Ala Pro Gly
                       20
gca gag cga cgg gac cgt gcc ctt ctg ggm cca cgc ggg gaa tgc tat
                                                                    243
Ala Glu Arg Arg Asp Arg Ala Leu Leu Gly Pro Arg Gly Glu Cys Tyr
                    35
                                       40
                                                           45
tcc aag ttc aga tca aat tcg agt agc acc atc ttt aaa aag cya aag
                                                                    291
Ser Lys Phe Arg Ser Asn Ser Ser Ser Thr Ile Phe Lys Lys Xaa Lys
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                                                                    327
agg ctc agt gtg gvm aam gac aav agc gga cct ggg
Arg Leu Ser Val Xaa Xaa Asp Xaa Ser Gly Pro Gly
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gaactcacc atg gag ttt ggg ctg agc tgg gtt ttc ctt gtt gct att tta
                                                                    111
          Met Glu Phe Gly Leu Ser Trp Val Phe Leu Val Ala Ile Leu
                          -15
aaa ggt gtc cac tgt gac gtg cag ctg gtg gag tcc ggg gga ggt tta
                                                                    159
Lys Gly Val His Cys Asp Val Gln Leu Val Glu Ser Gly Gly Leu
-5
gtt cag cct ggg ggg tcc ctg aga ctc tcc tgt gca gcc tct gga ctc
                                                                    207
Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Leu
                               20
            15
acc ctc agt aac gac tgg atg cac tgg gtc cgc caa gcc cca ggg aag
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Gly Leu val Trp Val Ser His Ile Asp Ser Ser Xaa Thr Ile Thr Asn 45 50 55 1ac gog gac toc gtg aag ggc cga ttc acc atc tcc aga gac aac gcc 777 Ala Asp Ser Val Lys Gly Arg Phe Tr Ile Ser Arg Asp Ash Ala 60 65 70 75 357 357 357 357 357 357 357 357 357		
45 50 55 tac gcg gac tcc gtg aag ggc cga ttc acc atc tcc aga gac aac gcc Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala 60 65 70 75 aag tgg Lys Trp <pre> <pre> <pre> <pre></pre></pre></pre></pre>		303
tac gcg gac tcc gtg aag gcg cas ttc acc atc tcc aga gac aac gcc Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala 60 65 70 75 aag tcg Lys Trp <pre> <210> 218 <211> 189 <212> DNA <213> Homo sapiens </pre> <pre> <220> <221> CCS <221> CCS <222> 74187 </pre> <pre> <221> sig_peptide <222> 7418 </pre> <pre> <a hre="</td"><td></td><td></td></pre>		
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Ctatcataga caa atg ggt tta ttt ctg ggc ttt cta gcc tgt tct gtt Met Gly Leu Phe Leu Gly Phe Leu Ala Cys Ser Val -15 -10 -15 gca tac cag tgc cat tct gct ttt gtt act gta gct tca cag tac act Ala Tyr Gln Cys His Ser Ala Phe Val Thr Val Ala Ser Gln Tyr Thr 1	ttatcaagga cactgtcttt tcgccatcat gtgttcttgg cccctctgtt gaaattcaat	60
-15	ctatcataga caa atg ggt tta ttt ctg ggc ttt cta gcc tgt tct gtt	109
gca tac cag tgc cat tet gct ttt gtt act gta gct tca cag tac act Ala Tyr Gln Cys His Ser Ala Phe Val Thr Val Ala Ser Gln Tyr Thr 1		
Ala Tyr Gln Cys His Ser Ala Phe Val Thr Val Ala Ser Gln Tyr Thr 1		157
ttg aaa tca gag act ttg atg ccc gca gcg gg Leu Lys Ser Glu Thr Leu Met Pro Ala Ala 15 20 <pre> <210> 219 <211> 353 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 41352 <pre> <221> CDS <222> 41352 </pre> <pre> <pre> <pre> <221> cgc 6.69999980926514</pre></pre></pre></pre>	Ala Tyr Gln Cys His Ser Ala Phe Val Thr Val Ala Ser Gln Tyr Thr	13,
Leu Lys Ser Glu Thr Leu Met Pro Ala Ala 15 20 <210> 219 <211> 353 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 41352 <222> 41187 <223> Von Heijne matrix	1 5 10	
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ctc g Leu G	ggt 3ly	ctc Leu -10	atc Ile	ttc Phe	ttc Phe	ctg Leu	gag Glu -5	ctg Leu	gca Ala	aca Thr	Gly ggg	atc Ile 1	ctg Leu	gcc Ala	ttt Phe	1	99
gtc t Val F 5	Phe	Lys	Asp	Trp	Ile 10	Arg	Asp	Gln	Leu	Asn 15	Leu	ttc Phe	Ile	Asn	Asn 20		47
aac g Asn V	gtc /al	aag Lys	gcc Ala	tac Tyr 25	cgg Arg	gac Asp	gac Asp	att Ile	gac Asp 30	ctc Leu	cag Gln	arc Xaa	ctc Leu	att Ile 35	gac Asp	2:	95
ttt g Phe A	gct Ala	cag Gln	gaa Glu 40	tac Tyr	tgg Trp	tct Ser	tgc Cys	tgc Cys 45	gga Gly	scc Xaa	gag Glu	gcc Ala	cca Pro 50	ata Ile	rdt Xaa		43
gga a Gly T	hr		g													3!	53
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gcc a Ala M 1	et :	ata Ile	att Ile	Tyr	tca Ser 5	gct Ala	ctc Leu	tct . Ser .	Ala	gga Gly 10	ttt Phe	att Ile	att Ile	Phe	ttt Phe 15	9	8
tta g Leu V			Phe :		ct								•			11	L5
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cta to	gg d		cc c				caa t	ct t	at a	att o	cct t	ct (tc 1	ttc (ctt	10	0

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tgccacaget tagttagett tgagagggaa agggtagaat ccatttaagg agacaggtta
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aaaaatgata tatttaagca tataggca atg gta gca cat gat tac caa aac
                                                                    232
                              Met Val Ala His Asp Tyr Gln Asn
                                      -25
ata att agc ctt ttc ttt ctt gct ttt tca ttt tct ttc ttt cct tct
                                                                    280
Ile Ile Ser Leu Phe Phe Leu Ala Phe Ser Phe Ser Phe Phe Pro Ser
               -15
                                   -10
                                                                    328
Ser Phe Ser Ser Phe Phe Leu Xaa Phe Leu Ser Phe Phe Ser Ser Phe
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Arg Gly Val Ala Ala Gln Val Leu Arg Xaa Gly Ala Gly Val Arg Leu
ccg att cag ccc agc aga ggt gtt cgg cag tgg cag cca gat gtg gaa
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Pro Ile Gln Pro Ser Arg Gly Val Arg Gln Trp Gln Pro Asp Val Glu
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ctg ggt gtg aag ccg agc acg cat tgg cta ttc ttc ctg atg ctc tcc Leu Gly Val Lys Pro Ser Thr His Trp Leu Phe Phe Leu Met Leu Ser -20 -15 -10	148									
ctt tgc acc cct cct gac aga ccc tgg tgt gtg ttg ttc ccc ccg ctg Leu Cys Thr Pro Pro Asp Arg Pro Trp Cys Val Leu Phe Pro Pro Leu -5 1 5 10	196									
99	198									
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-10 -5 ggg aag aga ggc Cag gca tqq cgg ctc atq cct gtw gtc cca gca gtt	160									

Gly Lys Arg Gly Gln Ala Trp Arg Leu Met Pro Val Val Pro Ala Val tgg gag cct gag gca ggt gga ttg ctt cag ctc ggg ggt tct agg g 206 Trp Glu Pro Glu Ala Gly Gly Leu Leu Gln Leu Gly Gly Ser Arg <210> 228 <211> 480 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 216..479 <221> sig_peptide <222> 216..326 <223> Von Heijne matrix score 6.5 seq LLVFFLIVRTLSC/RS <400> 228 qcatcccck ktagctcaga gaagtttgtt rdgaccgatc ttctgaagcc tacttctgtc aactcatcaa agtcattctc catccagctt tgttccatta tgggtgagga gctacgatcc. 120 tttqqaqqaq aagaggcact ctgattttta gaattttcag cttttctgct ctggtttcgc 180 cccatctttg tggttttatc taccttcggt ctttg atg atg gtg acc tac aga 233 Met Met Val Thr Tyr Arg. tgg ggt ttt ggt gtg gat gtc mtt ttt gtt gct gtt gat gct att cct 281 Trp Gly Phe Gly Val Asp Val Xaa Phe Val Ala Val Asp Ala Ile Pro -25 -20 ttc tgt ttg tta gtt ttc ttt cta ata gtc agg acc ctc agc tgc agg 329 Phe Cys Leu Leu Val Phe Phe Leu Ile Val Arg Thr. Leu Ser Cys Arg -15 -10 - 5 377 tet gtt gga gta tgc tgg agg tee aet cea gae eet gtt tge eta ggt Ser Val Gly Val Cys Trp Arg Ser Thr Pro Asp Pro Val Cys Leu Gly 10 425 atc acc agc aga ggc tgc aga aca gaa ata ttg cag aac agc aaa tgt Ile Thr Ser Arg Gly Cys Arg Thr Glu Ile Leu Gln Asn Ser Lys Cys 25 tgc tcc ctg atc ctt cct ctg gaa gct tcg tct caa agg ggc act gaa 473 Cys Ser Leu Ile Leu Pro Leu Glu Ala Ser Ser Gln Arg Gly Thr Glu 40 480 tgt atg a Cys Met 50 <210> 229 <211> 144 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 43..144 <221> sig peptide <222> 43..99 <223> Von Heijne matrix

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score 6.5

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ctg cct gag ata ttc tta cct ttt tct ttg tcc cca gca aat gcc cag
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Leu Pro Glu Ile Phe Leu Pro Phe Ser Leu Ser Pro Ala Asn Ala Gln
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Ser Lys Phe Ser Leu Tyr Phe Phe Pro Leu Val Lys Pro Gly
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                                                                      349
               Met Ser Leu Glu Pro Ala Ser Xaa Leu Leu Gly Val
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cgg cgg aga ctg ctt tgt cta mct ttc tsc cga ctt ctc tta ggr acc
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Arg Arg Arg Leu Leu Cys Leu Xaa Phe Xaa Arg Leu Leu Gly Thr
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Ser Leu Leu Lys Phe Val Xaa Ser Xaa Ser Pro Pro Xaa Pro Xaa Thr
ctc acc tct tcc
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Leu Thr Ser Ser
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ccc tgg cac ggt ggc ctg ctc caa ccg cta cct tgc tct ttc gag atg Pro Trp His Gly Gly Leu Leu Gln Pro Leu Pro Cys Ser Phe Glu Met 15 20 25 30	5
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<222> 339..392
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<222> 339..383.
<223> Von Heijne matrix
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                                                                        60
agatttgaac aacatggtaa tcatgtgatg gacatggaaa agtgractaa cbtkrqqqat
                                                                       120
cwtggtargg tcaytaagaa taactckaat cawgatgtta aaaggctttc ctttacattc
                                                                       180
acaaaacaat ttrsttccta gaagtagttt attcttgcct gtggtcattt ttgctccttt
                                                                       240
ataatactac atctaaatca atttgttaaa tatagtagag aaatgaaata aatttcttcc
                                                                       300
agttaaacca ctgcacttaa agagtagaaa ccctctct atg tca ctc ttt gtt ttg
                                                                       356
                                           Met Ser Leu Phe Val Leu
ttg atc ata act caa ctg ctg tat ggt ggg ata ctc t
                                                                       393
Leu Ile Ile Thr Gln Leu Leu Tyr Gly Gly Ile Leu
                 -5
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<211> 222
<212> DNA
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<220>
<221> CDS
<222> 121..222
<221> sig_peptide
<222> 121..204
<223> Von Heijne matrix
      score 6.40000009536743
      seq ILFLGVLLSASDL/CV
<400> 236
ttttgagtta atttttgtat aagttgtaag gattaggtca gggttcttaa gaaaaatatt
                                                                        60
gttttggtct atagatgtct cattgcttct gtgctatttg ttggaaaagc tgttcttcca
                                                                       120
atg aat tgc ttt tgc aat ttt gtc aaa acc agt gag gca tat atg att
                                                                       168
Met Asn Cys Phe Cys Asn Phe Val Lys Thr Ser Glu Ala Tyr Met Ile
                                 -20
ctg ttt cta ggt gtt cta ctc tct gca agt gat tta tgt gtc tat ccc
                                                                       216
Leu Phe Leu Gly Val Leu Leu Ser Ala Ser Asp Leu Cys Val Tyr Pro
                             -5
atc ggg
                                                                       222
Ile Gly
<210> 237
<211> 154
<212> DNA
<213> Homo sapiens
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<212> DNA

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 <221> sig_peptide
 <222> 54..95
 <223> Von Heijne matrix
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       seq SVILALWEAEAGG/SP
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 agtettttgc teetgtggtt aagattatte tgetaggetg etcaeggtgg etg atg
                                                                         56
 tct gta atc cta gca ctt tgg gag gcc gag gcg ggc gga tcg cct gag
                                                                        104
 Ser Val Ile Leu Ala Leu Trp Glu Ala Glu Ala Gly Gly Ser Pro Glu
              -10
                                  -5
 atc ggg agt tcg gga ccg gcc gca cca aca tgg aga agc ccc gtc cag
                                                                        152
 Ile Gly Ser Ser Gly Pro Ala Ala Pro Thr Trp Arg Ser Pro Val Gln
                          10
 gg
                                                                        154
 <210> 238
 <211> 439
 <212> DNA
 <213> Homo sapiens
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 <222> 255..437
 <221> sig_peptide
 <222> 255..341
 <223> Von Heijne matrix
       score 6.30000019073486
       seq LGCLLLAVRSSAT/VN
 <221> misc feature
 <222> 359..360,381
 <223> n=a, g, c or t
 <400> 238
 tcaccacaat caattttaga acattttcat catcccgaaa ataagccctg ttccctttag
                                                                         60
 ctgtcactcc ccactcctac cccccagccc tgtgcaataa tctactttct gtctttgaag
                                                                        120
 ctttgcctat tctggacatt ttgtataaaa gggtttgtgg aggatgtggt cttttgtgac
                                                                        180
 tggcttcttg aacttggcat agtgttttca aggttcaacc atgttgtagc acgtacgttc
                                                                        240
 ctttttatgg ccaa atg tac gga gag tcc aca ttg ttt atc cat tca tca
                                                                        290
                 Met Tyr Gly Glu Ser Thr Leu Phe Ile His Ser Ser
 gtt. cat ggg cat ttg ggt tgt ctc ctc ttg gct gtt agg agt agt gct
                                                                        338
 Val His Gly His Leu Gly Cys Leu Leu Leu Ala Val Arg Ser Ser Ala
                              -10
 act gtg aac att acg tac chn nkw gtk tgt gtg gac att cak ntt cat
                                                                        386
 Thr Val Asn Ile Thr Tyr Xaa Xaa Val Cys Val Asp Ile Xaa Xaa His
                                          10
 ttc cat atg ctt atg tct gga att act ggg tca tat ggc aac tct ctt
                                                                        434
 Phe His Met Leu Met Ser Gly Ile Thr Gly Ser Tyr Gly Asn Ser Leu
                 20
 tca ct
                                                                        439
 Ser
 <210> 239
 <211> 229
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<213> Homo sapiens
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<222> 7..228
<221> sig peptide
<222> 7..159
<223> Von Heijne matrix
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      seq WLYLLEVVAPLSG/IH
<400> 239
gtcaag atg gcg gcg tct gta tta aac acc gtg ctg agg cgg ctt cct
                                                                        48
       Met Ala Ala Ser Val Leu Asn Thr Val Leu Arg Arg Leu Pro
                               -45
atg cta tct ctc ttc cga ggt tct cac aga gtt cag gta act ctt cga
                                                                        96
Met Leu Ser Leu Phe Arg Gly Ser His Arg Val Gln Val Thr Leu Arg
        -35
                            -30
                                                 -25
aag aca ttt tgc aca acc tca agt tgg tta tac ctt ctc gag gtt gtc
                                                                       144
Lys Thr Phe Cys Thr Thr Ser Ser Trp Leu Tyr Leu Leu Glu Val Val
                        -15
                                             -10
get cea etg tea gga ate cae gag tgg aga eet tee cae gtg tgt ett
                                                                       192
Ala Pro Leu Ser Gly Ile His Glu Trp Arg Pro Ser His Val Cys Leu
                    1
age tgt cta ggc agt act tee tge aac eec eet gag g
                                                                       229
Ser Cys Leu Gly Ser Thr Ser Cys Asn Pro Pro Glu
<210> 240
<211> 318
<212> DNA
<213> Homo sapiens
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<221> CDS
<222> 65..316
<221> sig peptide
<222> 65..259
<223> Von Heijne matrix
      score 6.30000019073486
      seq LMVVAETSQGSWS/AP
<221> misc_feature
<222> 259
<223> n=a, g, c or t
<400> 240
ctcttcggtt gtccagccct tctcccagcc ctggtccctc agaaggaggg taactccctt
                                                                       60
ccag atg tta cgg tcc gcc tgc gtc tct cag cac gcc ggt ggc att tgg
                                                                      109
    Met Leu Arg Ser Ala Cys Val Ser Gln His Ala Gly Gly Ile Trp
                         -60
gtt gac cgc gga ggc ccc cag tgc cag agg gtg ttc acg ttc tgc cgt
                                                                      157
Val Asp Arg Gly Gly Pro Gln Cys Gln Arg Val Phe Thr Phe Cys Arg
                                        -40
ggg etc age eca aac ttt gga ege tea gag ace eaa egg gag ege tgg
                                                                      205
Gly Leu Ser Pro Asn Phe Gly Arg Ser Glu Thr Gln Arg Glu Arg Trp
                -30
                                    -25
ata agg cca gga cag ctg atg gtt gtg gca gaa aca tct caa ggt agc
                                                                      253
Ile Arg Pro Gly Gln Leu Met Val Val Ala Glu Thr Ser Gln Gly Ser
```

-10

-15

138 tgg ten gee eec act tee eea tst acc tet tgt eet eec eec aac acc Trp Ser Ala Pro Thr Ser Pro Xaa Thr Ser Cys Pro Pro Pro Asn Thr asc acc aca ccg gyt cc 318

Xaa Thr Thr Pro Xaa

<210> 241

<211> 405 <212> DNA

<213> Homo sapiens

<220>

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<222> 123..404

<221> sig_peptide

<222> 123..257

<223> Von Heijne matrix score 6.30000019073486 seq GFVSLLVVHAADA/WV

<400> 241

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Leu Asp Ser Glu Gly Ser Ser Ser Ile Xaa Pro Ser Thr Pro Phe

40

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<211> 242

<212> DNA

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<221> CDS

<222> 129..242

<221> sig peptide

<222> 129..191

<223> Von Heijne matrix score 6.30000019073486 seq SLLPCSLISDCCA/SN

<400> 242

cttttgtttt gcaatgccct gccccagag gtggagtcta cagaggcagg caggcctcct 60 tgagctgagg tgggctccac ccagttcgag cttcccagct gctttgttta cctactcaag 120 cctgggca atg gtg ggc gcc ctt ccc cca gcc tcg ctt ctg cct tgc agt 170

139	
Met Val Gly Ala Leu Pro Pro Ala Ser Leu Leu Pro Cys Ser -20 -15 -10	
ttg atc tca gac tgc tgt gct agc aat gag cga ggc tcc atg ggc gta Leu Ile Ser Asp Cys Cys Ala Ser Asn Glu Arg Gly Ser Met Gly Val -5 5	218
gga ccc tct gag cca cgg cgy ggg Gly Pro Ser Glu Pro Arg Arg Gly 10 15	242
<210> 243 <211> 363 <212> DNA <213> Homo sapiens	
<220> <221> CDS <222> 298363	
<221> sig_peptide <222> 298357 <223> Von Heijne matrix score 6.30000019073486 seq LGSLIASLAPSTG/LG	
<pre><400> 243 accactctga ggagacgcgt gacagataag aagggctggt gggatcagtc ctggtggtag ctcaggaagc agagcctgga gcatctccac tatggcctgg gctccactac ttctcaccct cctcgctcac tgcacaggtt cttgggccaa ctttatgctg actcagccgc actctgtgtc ggagtcgccg gssgaagacg gtaaccatct cctgcacccg cagcagtggc agctttgtca gcaactatgt tcagtggtac cagcggcgcc cggacagtgc ccccaccact gtgatct atg agg atg aca aaa gac cct ctg ggg tct ctg atc gct tct ctg gct Met Arg Met Thr Lys Asp Pro Leu Gly Ser Leu Ile Ala Ser Leu Ala -20 -15 -10 -5</pre>	60 120 180 240 297 345
cca tcg aca ggt ctt ggg Pro Ser Thr Gly Leu Gly	363
<210> 244 <211> 324 <212> DNA <213> Homo sapiens	
<220> <221> CDS <222> 153323	
<221> sig_peptide <222> 153236 <223> Von Heijne matrix score 6.30000019073486 seq FFLFLFFXEXXXX/XX	
<400> 244 aattgatact gctttagatg tttctgtctc attttacaaa aatgtaagaa aaaagaaaaa tcaaactata ctgttaccta tttcttgtat attcttaaca gaatgttctg tacacataag tgtatgtgtg ttaatcctct tgtttaaatg cc atg aaa ctt cag ttt gcc ttt Met Lys Leu Gln Phe Ala Phe -25	60 120 173
tgt tat ttt ctt tat tta gat acc ttt ttt ctt ttt ctt ttt ttk Cys Tyr Phe Leu Tyr Leu Asp Thr Phe Phe Leu Phe Leu Phe Phe Xaa -20 -15 -10	221
gag ama gyc tkg cyc kgt kgc hta ggm agg agt gca gtg gca maa cct Glu Xaa Xaa Xaa Xaa Xaa Xaa Gly Arg Ser Ala Val Ala Xaa Pro	269

140																
-5					1				· 5					10		
cag Gln	ctc Leu	ayt Xaa	gca Ala 15	gcc Ala	tcc Ser	acc Thr	ttc Phe	kgg Xaa 20	tty Phe	caa Gln	gca Ala	att Ile	tty Phe 25	ctg Leu	ccc Pro	. 317
	ckg Xaa	g														324
<213 <212	0> 24 L> 24 2> DI 3> He	0 8 NA	sapi	ens												
<220 <22])> l> CI															
<222	2> 2' 3> Vo	72: on H	eijno	e mai		73486	5									
400	s	eg G	ILKVI													•
	jeggg		9999	ectto	eg ca	agago	ato Met	g gcg	g gcg a Ala	g gg a Gl	c gag y Glu -69	ı Let	gag Glu	g ggt ı Gly	ggc Gly	53
Lys -60	Pro	Leu	Ser	Gly	Leu -55	Leu	Asn	Ala	Leu	Ala -50	cag Gln	gac Asp	Thr	Phe	His -45	101
31y 399	tac Tyr	ccc Pro	ggc Gly	Ile -40	aca Thr	gag Glu	gag Glu	ctg Leu	cta Leu ~35	cgg Arg	agc Ser	cag Gln	cta Leu	tat Tyr -30	cca Pro	149
gag Glu	gtg Val	cca Pro	ccc Pro -25	gag Glu	gag Glu	ttc Phe	cac His	ccc Pro -20	ttt Phe	ctg Leu	gca Ala	aag Lys	atg Met -15	agg Arg	999 Gly	197
att Ile	ctt Leu	aag Lys -10	gta Val	ctg Leu	ctc Leu	ttt Phe	tct Ser -5	gta Val	gtc Val	tcc Ser	ggc Gly	ttg Leu 1	gag	cag Gln	aac Asn	245
ecc Pro	ttg Leu	gcc	gct Ala	ggc Gly	ttc Phe 10	aga Arg	ctc	tcc Ser	cac His	ccg Pro 15	gg	•				280
<211 <212	> 24 > 21 > DN > Ho	.1 IA	apie	ens												
	> CI	os)21	.0													
<222	> 70 > Vc sc	on He core	ijne	mat	1907	3486 FF									·	
ttg	> 24 gctg aagg	gg g t at	g at	g at	g to	a aa	c gt	g at	g ct	gat	g ct	a ca	g tt	a ca	tccac g ccc n Pro	111
·+~	ata		-3					-2					-2			

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Leu Leu Ala Xaa Ser Leu Ile Leu Ser Pro Ser Pro Arg Pro Val Leu
        -15
                             -10
ggc ttt ttc aga caa gtg cat ctc cta acc agg tca cat ttc agc cgc
                                                                       207
Gly Phe Phe Arg Gln Val His Leu Leu Thr Arg Ser His Phe Ser Arg
                                         10
tgg g
                                                                       211
Trp
<210> 247
<211> 359
<212> DNA
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<221> CDS
<222> 249..359
<221> sig_peptide
<222> 249..308
<223> Von Heijne matrix
      score 6.19999980926514
      seq LLFICPPPPPISA/SS
<400> 247
tttcagaatt ttgtgcagga atatctgagt atttctaatt agattagaat gtcagaatac
                                                                        60
attcatggac atatgagggg ttttttaaaa ttttttttag atatccttca ccttgaacat
                                                                       120
ttattatttc tttgtgttgg gaacaatcca aatctctcct agatgttttg aaatgtgcaa
                                                                       180
tgtattgtta gctgtagtca ccctactgtg ctattgaata ctagagcttg ttccttctgt
                                                                       240
ctaactgt atg att ata ctc att aac caa ctt ctc ttc atc tgt ccc cca
                                                                       290
         Met Ile Ile Leu Ile Asn Gln Leu Leu Phe Ile Cys Pro Pro
         -20
                             -15
cet cca ccc atc tca gcc tct agt aac tac cat ttt act ctc tac ctc
                                                                       338
Pro Pro Pro Ile Ser Ala Ser Ser Asn Tyr His Phe Thr Leu Tyr Leu
                                        5
cat gac att aac ttt ttt agc
                                                                       359
His Asp Ile Asn Phe Phe Ser
                15
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<222> 182..235
<221> sig peptide
<222> 182..226
<223> Von Heijne matrix
      score 6.19999980926514
      seq DVLLQLLLRVCSP/RT
<400> 248
attgggttaa tttcactgca ctgactattt ttagatatat attctttgtg ccttcactag
                                                                       60
aactcctctt acttcatgat atcttaacta taaaatcatc caaccatgaa aacaagcaca
                                                                      120
caagaaacag aaacaaaaca gtcacaaaaa agcataaact gttagcattg atccatgatg
                                                                      180
a atg act gat gta tta ctt caa ttg cta tta aga gtg tgt tct ccc agg
                                                                      229
 Met Thr Asp Val Leu Leu Gln Leu Leu Leu Arg Val Cys Ser Pro Arg
 -15
                      -10
acc agg g
                                                                      236
Thr Arg
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<210> 249 <211> 342 <212> DNA

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<220>
<221> CDS
<222> 266..340
<221> sig peptide
<222> 266..304
<223> Von Heijne matrix
      score 6.19999980926514
      seq MGLFLCCSLLIFC/LV
<400> 249
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gtcaatccat cttgagttca tttttgtata tgatgaaaag taggggtctg attttattct
                                                                       120
tctgcataag accagttatc ccagaaccgt ttgttgaata ggaagttctt ttctcattgc
                                                                      180
ttgtttgtgg ggactttgtc aaagatcaaa tagttatagg tgtgtggctg tatttcaggg
                                                                      240
tttctttatt ccatttcact gatct atg ggt ctg ttt ttg tgc tgc tct tta '
                                                                      292
                            Met Gly Leu Phe Leu Cys Cys Ser Leu
                                         -10
ctg ata ttc tgt ctg gtt gtt cta atc ata act gaa ctg ggc tat ggg
                                                                      340
Leu Ile Phe Cys Leu Val Val Leu Ile Ile Thr Glu Leu Gly Tyr Gly
                1
                                5
99
                                                                      342
<210> 250
<211> 382
<212> DNA
<213> Homo sapiens
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<222> 291..380
<221> sig_peptide
<222> 291..332
<223> Von Heijne matrix
      score 6.19999980926514
      seq GSWALTWLHPAEA/GT
<221> misc feature
<222> 264..265,279..280
<223> n=a, g, c or t
<400> 250
atacagegge ctctgacace agcacageaa accegeeggg atcaaagtgt accagtegge
                                                                       60
agcatgggta aggagaggg tttccaatca cccattgcct gctctgtctg cccctaattt
                                                                      120
ggaaaggccc tcctccagaa aatgctagaa aacctgagtg gggagctggg gagggagtag
                                                                      180
tggactctgc ttcattgtcc ccagtctgca cacccctcc cccaccaccc cactgcattt
                                                                      240
cccagctcag ccaaactttc tgannaagac gggcagagnn ctgctgggag atg gga
                                                                      296
                                                        Met Gly
tee tgg gee etg aet tgg ete eat eea gea gag get ggg aee agg gtg
                                                                      344
Ser Trp Ala Leu Thr Trp Leu His Pro Ala Glu Ala Gly Thr Arg Val
        -10
                            -5
cct ttc tgc agc tgg gaa aaa tca gat ggg cgc tct ta
                                                                      382
Pro Phe Cys Ser Trp Glu Lys Ser Asp Gly Arg Ser
                    10
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143
 <211> 303
 <212> DNA
 <213> Homo sapiens
 <220>
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 <222> 108..302
 <221> sig_peptide
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      seq LSVLSLVINFSWS/RK
<221> misc_feature
 <222> 279
<223> n=a, g, c or t
<400> 251
aaaagctgtg aggttgtaac tcagttcagt agtatttata aatatttgtt ttccactttt
                                                                        60
gtgcatatta tacaaatgat ggatataaaa tttgtttwga ccatwta atg atg ctt
                                                                       116
                                                     Met Met Leu
rmw wwr rra aga gga tat cct cat aga act gaa cgt tat gat gga ttt
                                                                       164
Xaa Xaa Xaa Arg Gly Tyr Pro His Arg Thr Glu Arg Tyr Asp Gly Phe
                 -35
                                     -30
tta aaa tat tot gac cca aat gat att gca ttg tca gta ctg tcc ctg
                                                                       212
Leu Lys Tyr Ser Asp Pro Asn Asp Ile Ala Leu Ser Val Leu Ser Leu
            -20
                                 -15
                                                     -10
gtt att aat ttc tcc tgg agt aga aaa tgc ttt gtt cct tac tat atc
                                                                       260
Val Ile Asn Phe Ser Trp Ser Arg Lys Cys Phe Val Pro Tyr Tyr Ile
cca ttt aaa cct tac cgv nta cct tac ccc acc gcg gcc cgg g
                                                                       303
Pro Phe Lys Pro Tyr Arg Xaa Pro Tyr Pro Thr Ala Ala Arg
                    15
<210> 252
<211> 259
<212> DNA
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<222> 106..258
<221> sig_peptide
<222> 106..222
<223> Von Heijne matrix
      score 6.19999980926514
      seq CFVCXLFVFLLSG/LN
<221> misc feature
<222> 134
<223> n=a, g, c or t
<400> 252
atttaaaagg attttttaaa ggacctctat agttataagt cagcttaatt aaaaatggat
attecatagt catatttata tatatataca cacacatata tatgt atg tat gtg tgt
                                                                      117
                                                  Met Tyr Val Cys
ata tat ata trt tta ana gac ctg tat gat ttt ttt ctt ctt gga act.
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Ile Tyr Ile Xaa Leu Xaa Asp Leu Tyr Asp Phe Phe Leu Leu Gly Thr

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gacyctgynw haaatcmtgt gaagyhatgc agahcatctg gacacagctt tctccagcag
ggatyyatdg ttttgggctt gaaggggttt cacggctttt tctataacaa cg atg gca
                                                           Met Ala
                                                               -25
tot toa atg ctg waa too tto cag act tto atg atg ttg act cta ttg
                                                                      286
Ser Ser Met Leu Xaa Ser Phe Gln Thr Phe Met Met Leu Thr Leu Leu
                -20
                                    -15
                                                        -10
ggt ttc cct tcc aaa gct ttg aca ttc att tcc a
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Gly Phe Pro Ser Lys Ala Leu Thr Phe Ile Ser
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tataaagaag tgtaaacagg aaagccagct gggcctggag ttccaagtgc ccatatttca
                                                                      120
tragetteet etecataact gtggcaggga caettaacce tteeetgget gtgagaagtt
                                                                      180
attetetgag ggetggtgag caga atg gga aga tet aag agg cag etc ett
                           Met Gly Arg Ser Lys Arg Gln Leu Leu
                           -20
                                                -15
tcc ttg cct ggt tcc ttt atc cct ggg aat tgc agg cca agg att ctg
                                                                      279
Ser Leu Pro Gly Ser Phe Ile Pro Gly Asn Cys Arg Pro Arg Ile Leu
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agc aat ggw gaa gwc aga agg aag gg
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-30 -25 -20	-ne
ttc acc cag tgc tgc ctt att gga ctc ctt gtg cct ctc ctt ggc t Phe Thr Gln Cys Cys Leu Ile Gly Leu Leu Val Pro Leu Leu Gly 7 -15 -10 -5	tgg 217 Frp
gga aat cag aat aca cag tgg tat ccc act tct aag atg cct gat g Gly Asn Gln Asn Thr Gln Trp Tyr Pro Thr Ser Lys Met Pro Asp G	ggg 265 Gly LS
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Met Gly Arg Ser -30	Asn
gat ttt agg ttt gcc ttt cta aca tgc ttt ctt gga tgg gaa ata g Asp Phe Arg Phe Ala Phe Leu Thr Cys Phe Leu Gly Trp Glu Ile V -25 -20 -15	ta 224 al
tat ttc ttg gtg ctt ctt cgt gtt tta tac act tta caa tgg ggt g Tyr Phe Leu Val Leu Leu Arg Val Leu Tyr Thr Leu Gln Trp Gly G -10 -5 1 5	ly
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cagcaatccc attgctaggt atataccccc ccaaaaaagg aaatcagtat atgaaagaga
                                                                       120
tatetgaate ee atg ttt ett gea gea etg ttt aca gta get aag att tgg
                                                                       171
              Met Phe Leu Ala Ala Leu Phe Thr Val Ala Lys Ile Trp
                              -10
aag caa cct aag tgt tca tca aca aac aaa tgg aca aag aaa atg tgg
                                                                       219
Lys Gln Pro Lys Cys Ser Ser Thr Asn Lys Trp Thr Lys Lys Met Trp
                    5
                                         10
tac ata tac aca atg gag tac tat tca gcc ata aaa aaa gat gat atc
                                                                       267
Tyr Ile Tyr Thr Met Glu Tyr Tyr Ser Ala Ile Lys Lys Asp Asp Ile
                                     25
ctg tca ttt gca aca ata tgg atg gaa ctg gag agc att aca tta agt
                                                                       315
Leu Ser Phe Ala Thr Ile Trp Met Glu Leu Glu Ser Ile Thr Leu Ser
            35
                                40
gaa ata agt ggg sca cca aaa gac aaa ctt ctc atg ttc tca ctc att
                                                                       363
Glu Ile Ser Gly Xaa Pro Lys Asp Lys Leu Leu Met Phe Ser Leu Ile
                            55
                                                 60
tgt gga ag
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Cys Gly
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gtasecogge catggetetg tagectegae ecetttgtge ecceggeeeg teteegeget
                                                                       120
caccacgeet gegeteteeg eteccacett etttetteag eegaggeege egeegeetet
                                                                       180
cottgetgea gee atg gag tot toe act the gee thig gtg eet gte the
                                                                       229
               Met Glu Ser Ser Thr Phe Ala Leu Val Pro Val Phe
                       -25
gcc cac ctg agc atc ctc cag agc ctc gtg cca gct gct ggt gca gyc
                                                                       277
Ala His Leu Ser Ile Leu Gln Ser Leu Val Pro Ala Ala Gly Ala Xaa
-15
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tct cct
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Ser Pro
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                                                                       120
tataaattac ctctcaaaca aatgggccat tcagaarnrg gctcagagtg aattagctgg
                                                                       180
aggggttgtc aagggtcata gtttttactg ctttgaagag attatcactg g atg att
                                                                       237
tee tea cat tta tat aac tte agt ete etg tte ttt kta ete tgg etg
                                                                       285
Ser Ser His Leu Tyr Asn Phe Ser Leu Leu Phe Phe Xaa Leu Trp Leu
    -20
                         -15
agg tac aag gaa tca gga aga gag ggc aac tgt gag gaa gga gca ttc
                                                                       333
Arg Tyr Lys Glu Ser Gly Arg Glu Gly Asn Cys Glu Glu Gly Ala Phe
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tcc agg tgg
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Ser Arg Trp
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g atg ggg tgg cag cga ctc cta ctg ctg cct cgg cct cct gcc agt aca
                                                                      109
  Met Gly Trp Gln Arg Leu Leu Leu Pro Arg Pro Pro Ala Ser Thr
          -15
                              -10
ggt gca tcg aat gca acc agg rrg cca aag agk ttg tac cga grc tat
                                                                      157
Gly Ala Ser Asn Ala Thr Arg Xaa Pro Lys Xaa Leu Tyr Arg Xaa Tyr
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aac cac ggt gtg ctg aag ata acc atc tgt aaa tcc tgc cag aaa cct
                                                                      205
Asn His Gly Val Leu Lys Ile Thr Ile Cys Lys Ser Cys Gln Lys Pro
                20
                                    25
gta gac aaa tat atc gag tat gat cct gtt atc atc ttg awk aat gct
                                                                      253
Val Asp Lys Tyr Ile Glu Tyr Asp Pro Val Ile Ile Leu Xaa Asn Ala
                                40
ata ttg tgc aaa gct cad gcc tac agr cat att ctt ttc aat act caa
                                                                      301
Ile Leu Cys Lys Ala Xaa Ala Tyr Arg His Ile Leu Phe Asn Thr Gln
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                                                                       108
 Met Arg Gly Ala Trp Ile Ser Ile Phe Leu Ser Ser Leu Ser Leu Ser
             -15
 ctc tct ctt ttt t
                                                                       121
 Leu Ser Leu Phe
         1
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                                                                       120
 acaatatgaa tttcttttat ctgtcaatct caaggtagaa ttcctcatat ttctgataat
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 gccaaatacc atgaa atg tct caa aaa aga ctt gac ttt ata tac cag ttg
                                                                       231
                  Met Ser Gln Lys Arg Leu Asp Phe Ile Tyr Gln Leu
                                   -20
 ttt gtc ttg ctg cct cac ttc ttc ctt tct ttt ctt tct ccc ttt tat
                                                                       279
 Phe Val Leu Leu Pro His Phe Phe Leu Ser Phe Leu Ser Pro Phe Tyr
                             -5
 ctg cac cca tgg g
                                                                       292
 Leu His Pro Trp
 5
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  Met Tyr Leu Tyr Leu Leu Ser Ile Cys Met Ser Ser Leu Lys Lys Cys
              -30
                                   -25
                                                                        97
cta ttc aag ttc tta gcc cac ttt tta atc ggg tta aca gtt tgt ttt
Leu Phe Lys Phe Leu Ala His Phe Leu Ile Gly Leu Thr Val Cys Phe
        -15
                            -10
                                                 -5
ggt gag ggr wgg cta atg agt tat agg agt tct tat tta tta ctt aaa
                                                                       145
Gly Glu Gly Xaa Leu Met Ser Tyr Arg Ser Ser Tyr Leu Leu Leu Lys
                                         10
                                                             15
                                                                       158
gga cca ccg ggg g
Gly Pro Pro Gly
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                                                                        54
                                  Met Gly Phe Trp Cys Glu Cys Pro
                                          -20
                                                                       102
tto tgt ttg tta gtt tto ctt cta aca gag tgg acc tct agc aaa ctc
Phe Cys Leu Leu Val Phe Leu Leu Thr Glu Trp Thr Ser Ser Lys Leu
                 -10
                                     -5
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caa aag acg gg
Gln Lys Thr
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agaagaatgg caaggctaac agggcaggtg teegggegga ggggeggaac tggetgttgg
c atg tgg tgg ggg aga tgc ttc atc cgg gtc ttg cat ttg ttc cct ctg
 Met Trp Trp Gly Arg Cys Phe Ile Arg Val Leu His Leu Phe Pro Leu
          -20
                              -15
aca cca gcc tcg aca gga cac tgg g
                                                                      254
Thr Pro Ala Ser Thr Gly His Trp
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                                                                      120
catatttatt ttgagataat taacgaagac gttaaataaa gccagactgc actgacccct
                                                                      180
ggggcgcc atg cga gac ccc ctc gcg gac atg gta cac agt tat tta tca
                                                                      230
        Met Arg Asp Pro Leu Ala Asp Met Val His Ser Tyr Leu Ser
                         -25
teg tet ttg tte atg gee ett eea eea gtg etg age tea eat gge age
                                                                      278
Ser Ser Leu Phe Met Ala Leu Pro Pro Val Leu Ser Ser His Gly Ser
                    -10
agg aac ctg aga atc tgg ggg agt cca ttt ggt gga gcg ctg act aag
                                                                      326
Arg Asn Leu Arg Ile Trp Gly Ser Pro Phe Gly Gly Ala Leu Thr Lys
ggc aaa gca ccc cca acc cca gca caa cca gcc ctg gg
                                                                      364
Gly Lys Ala Pro Pro Thr Pro Ala Gln Pro Ala Leu
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                                                   Met Ser Ser Ala
tgg ctg tgt ctg cca tgc tcc ctg tgt gtg tcc cag ctc ctt ccc tct
                                                                      105
Trp Leu Cys Leu Pro Cys Ser Leu Cys Val Ser Gln Leu Leu Pro Ser
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Thr Ser Tyr Cys Arg Ser Ala Thr Leu Val Gly Phe Thr Val Gly Ser -15 -10 -5	
gtc cta ggg caa atc ctt gtc tca gtg gca ggc tgg tcg ctg ttc agc Val Leu Gly Gln Ile Leu Val Ser Val Ala Gly Trp Ser Leu Phe Ser 1 5 10	2
ctg aat gtc atc tct ctt acc tgt gtt tca gtg gct ttt gct gtg gcc Leu Asn Val Ile Ser Leu Thr Cys Val Ser Val Ala Phe Ala Val Ala 15 20 25	0
tgg ttt tta cct atg cca cag aag agc ctc ttc ttt cac cac att cct 248	8
Trp Phe Leu Pro Met Pro Gln Lys Ser Leu Phe Phe His His Ile Pro 30 45	
tct acc tgc cag aga gtg aat ggc atc aag gta caa aat ggt ggc att Ser Thr Cys Gln Arg Val Asn Gly Ile Lys Val Gln Asn Gly Gly Ile,	6
50 55 60 gtt act gac acc cag ctt cta aca cct tcc tgg ctg gga g 336	6
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12237 II-a, g, C OI C	
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actctaaaaa atctgggtat tgaggaarca tagctcaaaa gtgatgrgct gtttttgtac 180	0
cagtatcatg ctgttttggt tactgtagcc ctgtagtata gtttgangtt gggtaac 237 atg atg cct cca gct ttg ttc ttt ttg ctg agg att gct tgg cta tta 285	
Met Met Pro Pro Ala Leu Phe Phe Leu Leu Arg Ile Ala Trp Leu Leu -15 -5	-
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Met Thr Met Tyr	Leu Trp Leu	Lys Leu Leu	Ala Phe Gly Phe Ala	168
-15		-10	-5	•
Phe Leu Asp Thr Glu	gta ttt gtg	aca ggg caa	agc cca aca cct tcc Ser Pro Thr Pro Ser	216
1	5	ini diy din	10	
ccc act ggt gtt tca	tca gta cag	acg ccc cag	gg	251
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	20	. 25		
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gccaggag atg aca gca ctg ggg ttt gtt ctg tta gct cca cgt ggc tgg	170
Met Thr Ala Leu Gly Phe Val Leu Leu Ala Pro Arg Gly Trp -15 -10 -5	
ggg agc ctc aca gtc atg gtg gaa ggc aag gaa gag caa gtc acg tct	218
Gly Ser Leu Thr Val Met Val Glu Gly Lys Glu Glu Gln Val Thr Ser	
1 5 10 15	
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Tyr Thr Asp Gly Ser Arg Gln Arg Asp Ser Asn Phe 20 25	
	
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attactgtct tcagaaaact catgatgatc ctggccatga atg aaa agg ata aga	180 235
Met Lys Arg Ile Arg	233
-35	
aga aag aga aga aat gaa gtg acc atc cag cct ttc cca att aga ctt	283
Arg Lys Arg Arg Asn Glu Val Thr Ile Gln Pro Phe Pro Ile Arg Leu	
-30 -25 -20	
Pro Ley Loy Pro Pro Loy Ile Cor Phe Loy Win The Loy Pro Ley Loy Pro Ley Ile Cor Phe Loy Win The Loy Pro Ley Ile Cor Phe Loy Win The Loy Pro Ley Ile Cor Phe Loy Win The Loy Pro Ley Ile Cor Phe Loy Win The Loy Phe Loy Phe Loy Win The Loy Phe Loy Win The Loy Phe Phe Loy Phe	331
Pro Leu Leu Pro Pro Leu Ile Ser Phe Leu His Thr Leu Gln Val Val -15 -10 -5	
tgt tot gtg ata atg aaa agc atc aga aaa gct ttt gta ctt tgt ggt	379
Cys Ser Val Ile Met Lys Ser Ile Arg Lys Ala Phe Val Leu Cys Gly	313
1 5 10	
tto oto tat tit gaa tit tit gat caa aaa otg at	414
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                                                  Met Ala Ala Leu
cga agt act cta aca tgg aca gaa gtc gtg ggc tgg tgg agt gtt gcg
                                                                       163
Arg Ser Thr Leu Thr Trp Thr Glu Val Val Gly Trp Trp Ser Val Ala
                 -20 ·
                                      -15
teg ctg ctt agt gat gtg gca gca tgg tgg cca ccg cac tcc acc tca ,
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Ser Leu Leu Ser Asp Val Ala Ala Trp Trp Pro Pro His Ser Thr Ser
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aca cgg gga ggg gta
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Thr Arg Gly Gly Val
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gatggagaga gggacagagg gatggacgg atg aat gca ttr gta gat ggg aaa
                                                                      113
                                Met Asn Ala Leu Val Asp Gly Lys
cgg ctt asa krg tgc ata cgc tat ttc gat tct atc tca cta tat tct
                                                                      161
Arg Leu Xaa Xaa Cys Ile Arg Tyr Phe Asp Ser Ile Ser Leu Tyr Ser
                        -30
                                            -25
aag gca agt tta agt tgt tgt tta gtg tgt gtg ttt act tgt tca ttg
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Lys Ala Ser Leu Ser Cys Cys Leu Val Cys Val Phe Thr Cys Ser Leu
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                                        -10
cta gct ttc ttc agc cca tgc ac
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Leu Ala Phe Phe Ser Pro Cys
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gta cag cca ggg cgg tcc Val Gln Pro Gly Arg Ser 15	Leu Arg	Leu Ser Cys	Arg Thr Ser 25	Gly Phe
gcc ttt gat gat tat aas Ala Phe Asp Asp Tyr Ass 30	Leu Ser 35	Trp Val Arg	Gln Ala Pro 40	Gly Lys
ggg ctg gag tgg gta ggl Gly Leu Glu Trp Val Gly 45	Phe Ile . 50	aga agc aaa Arg Ser Lys	cct tat ggt Pro Tyr Gly 55	gag aca 240 Glu Thr
aca acg tac gcc gcg tgc Thr Thr Tyr Ala Ala Trp 60 65	•			258
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cttccattct ccatgttgtc tttttattct cttgatggta ttctttgaaa tacaaaartk

120

180

240

tttatatttg acaaagttca gtttatttat ttatttattg ccattcgtgc ttttggtttt . gataatccat ttttwttgtt tttattttta tttacttaga g atg ggg tct ccc tat Met Gly Ser Pro Tyr gtt gcc cac gtt ggt ctt gaa ctc ttg acc tca agt gat cct ccc tcc 464 Val Ala His Val Gly Leu Glu Leu Leu Thr Ser Ser Asp Pro Pro Ser -15 -10 ttg gcc tcc caa gtg ctg gga ata cat tm 493 Leu Ala Ser Gln Val Leu Gly Ile His <210> 305 <211> 214 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 79..213 <221> sig_peptide <222> 79..135 <223> Von Heijne matrix score 5.69999980926514 seq VCWLTLTLAHSHS/LT <400> 305 cacacacgca ccaaatacac acagasaccc tggccctcac tcacgcacav tctctcacac 60 tegtggacac acceccag atg cat ett tac act cat gta tge tgg etc act 111 Met His Leu Tyr Thr His Val Cys Trp Leu Thr -15 ctc aca ctg gca cac tca cac agc ttg acc cac acg cac aca ctc aca 159 Leu Thr Leu Ala His Ser His Ser Leu Thr His Thr His Thr Leu Thr -5 1 ecc agt cac aca egt aca cac tea cat acg tgt get tge eta cac gea 207 Pro Ser His Thr Arg Thr His Ser His Thr Cys Ala Cys Leu His Ala 15 20 cac aag g 214 His Lys 25 <210> 306 <211> 458 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 306..458 <221> sig_peptide <222> 306..350 <223> Von Heijne matrix score 5.69999980926514 seq LSLTFYHFPLCWG/HQ <221> misc_feature <222> 286,448 <223> n=a, g, c or t

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180 agaatctcct aaatgaagca tttggaatat tgattagtat accagaa atg gtt ttt 236 Met Val Phe ctt ttt ctt atg atc agc gtt ttt gcc ggt tgt caa atc cct tcc ggg 284 Leu Phe Leu Met Ile Ser Val Phe Ala Gly Cys Gln Ile Pro Ser Gly

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Asn

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aatagtotgg goatgatggt gtgcacctat agtotocago tabtoasgag cotgaggcag
                                                                       120
gaggwtcact tgagctkagg agttcaagga tgcagtsacc tgtgattgca ccactgcatt
                                                                       180
ccagcttgga caacagagtg agaccctgtc ttaaaattta aattttktgt yttwtggtag
                                                                       240
ag atg ggg tot ege cot gtt tee gak get ggt ete gaa ete etg gee
                                                                       287
   Met Gly Ser Arg Pro Val Ser Xaa Ala Gly Leu Glu Leu Leu Ala
       -20
                           -15
teg age aat tet tet gee tig eee tie caa tigt tet gigg att aca gige
                                                                      335
Ser Ser Asn Ser Ser Ala Leu Pro Phe Gln Cys Ser Gly Ile Thr Gly
atg agc crc cac acc cta gcg g
                                                                      357 .
Met Ser Xaa His Thr Leu Ala
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                                                                       60
aatcaaattt aataatatca agcttgcttg gtgagcatgg atttataaga tagaatggtt
                                                                      120
tgtgggggrg artatagtka cgaaaaagrk tattgtttcc cataatgcct ggtattgtat
                                                                      180
taagtacttt gcatacagta gggcatttca ttgtcccagt gatcctcctg caaagtaggt
                                                                      240
acaattatct tcaatttaca aatgaggaaa ccaagctctc ttcaagctga taagatgctg
                                                                      300
aactgagatt tgaaccaagt ccctctgccc ctaagagccc ctacccctag ctgctactat
                                                                      360
atgctgtacc catctaagct ttgtgaaata recttgttee actgcagaga ag atg ttg
                                                                      418
tgt cac cta tct cta gta ttt ctt ggc ktt ggg cag ttc tgg agt caa
                                                                      466
Cys His Leu Ser Leu Val Phe Leu Gly Xaa Gly Gln Phe Trp Ser Gln
    -10
aat g
                                                                      470
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 tggaggetee ttgtgatttt taatttgeae ttetgta atg act aat ett tte atg
                                                                        115
                                           Met Thr Asn Leu Phe Met
                                                   -15
 tgc ttg ttt gcc atc tgt ata tct tct aat gcg aag tgt ctg ttt agt
                                                                        163
 Cys Leu Phe Ala Ile Cys Ile Ser Ser Asn Ala Lys Cys Leu Phe Ser
                         -5
 ctt ttt cct ttt ttt att gag ggg
                                                                        187
 Leu Phe Pro Phe Phe Ile Glu Gly
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                                                                         60
 acataatctg ttcattgtta aacgtatacg aa atg ttg gga tac atc tgg naa
                                                                        113
                                     Met Leu Gly Tyr Ile Trp Xaa
 caa gac aaa gtc ttt gct aat tgt gtt cta ttt acg ctc tta gtg tct
                                                                        161
 Gln Asp Lys Val Phe Ala Asn Cys Val Leu Phe Thr Leu Leu Val Ser
 -20
                     -15
                                          -10
                                                               -5
 aca aga tee ggg aga teg egs geg ggt tgt gee tgg agg tgg agg gga
                                                                        209
 Thr Arg Ser Gly Arg Ser Arg Ala Gly Cys Ala Trp Arg Trp Arg Gly
 aga tgg tca gta gga cag aag ggc hgg g
                                                                        237
 Arg Trp Ser Val Gly Gln Lys Gly Xaa
         15
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 aagaggggaa agcccagggg tacaggaggc ctctgggtga aggcagaggc taacatgggg
                                                                       120
 ttcggagcga ccttggccgt tggcctgacc atctttgtgc tgtctgtcgt cactatcatc
                                                                       180
 atotgottca cotgotoctg otgotgoott tacaagacgt geogoogacc acgtocggtt
                                                                       240
gtcaccacca ccacatccac cactgtggtg c atg nnc ctt atc ctc agc ctc
                                                                       292
                                    Met Xaa Leu Ile Leu Ser Leu
                                    -15
 caa gtg tgc cgc cca gct acc ctg gac caa gct acc agg gct acc aca
                                                                       340
Gln Val Cys Arg Pro Ala Thr Leu Asp Gln Ala Thr Arg Ala Thr Thr
             -5
cca tgc cgc cta cgg g
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Pro Cys Arg Leu Arg
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                                             Met Cys His Arg Arg
                                                     -35
tgg ctg cac cta tca acc cgt cat cta ggt ttt aag ccc cgc atc cat
                                                                       102
Trp Leu His Leu Ser Thr Arg His Leu Gly Phe Lys Pro Arg Ile His
                             -25
tac gta ttt gtc tta atg ctg tcc ctc ccc ttg ccc ccc acc ccc caa
                                                                     . 150
Tyr Val Phe Val Leu Met Leu Ser Leu Pro Leu Pro Pro Thr Pro Gln
                         -10
     -15
cag gcc ctc ggg
                                                                       162
Gln Ala Leu Gly
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                                                                       120
aagcgtggac agaggaagtt ttaggtttga tttgaacttc atgtacatga catatttcat
                                                                       180
tttttttttt tccctcacaa atttcaaccc aggccacttg tttgcagaga ctgccaaacc
                                                                       240
ttccattgct gcttccaaga tactcctgga atctgagatt accttttatc ctcttg atg
                                                                       299
gac cat gtt gtt att ttt gtc att ttc cct gca gct ctt ctg ctt tgc
                                                                       347
Asp His Val Val Ile Phe Val Ile Phe Pro Ala Ala Leu Leu Cys
            -15
                                 -10
tgg gga gga ctc atc ccc cta tgc atc atc tac ccc ccg ata gct gac
                                                                       395
Trp Gly Gly Leu Ile Pro Leu Cys Ile Ile Tyr Pro Pro Ile Ala Asp
aca gtt ggg
                                                                       404
Thr Val Gly
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                                                                       120
gtgtatatat aacataaaca atacattaac ccaattttgt gtgaaaatta ttttgggacc
                                                                       180
tagtagcttt cttggtcaca acctttcaaa caaacaaatt ttttttaaat taattttttc
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ccttaataaa gaaaacaatt cctcaatgtg taatagcaaa taccttttaa caggtcatat
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atcatcaatg ctttctttga aancgtactg atgcttacaa gatgctttac gagtaaag
                                                                       358
atg ctt aca aat ctt ttc ttt caa gta gct cat cct ctg atc att att
                                                                       406
Met Leu Thr Asn Leu Phe Phe Gln Val Ala His Pro Leu Ile Ile Ile
                    -20
                                         -15
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ctg ntg ttt gat atc tac tcc cta gca ttt atc cat gac gtg gg

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                                                                       120
aacatcatta ttaaccagtg tcctattaaa actccttttc tatgatagaa tgtctgttrc
                                                                       180
ttttaggtgg ataaggccta gatgattggc ctctaccagc atcctcatct ctgtccctga
                                                                       240
tgcccagctt carceteget cetgyatget ggacegette agtghagete teagacttge
                                                                       300
tetgtgtete ac atg cty ttt gge tta egt gga atg ete eea ete ace eag
                                                                       351
              Met Leu Phe Gly Leu Arg Gly Met Leu Pro Leu Thr Gln
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caa gct ccc att cct cat tta aga tgt aaa ttg agt gtc acc tc
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                                                                       52
                     Met Arg Val Cys Met Arg Leu Cys Ala Cys Val
                         -20
                                              -15
tat gcg tgt gtg tgc gca tca gtg tct gca tgt gtg tat rtg tgt gta
                                                                       100
Tyr Ala Cys Val Cys Ala Ser Val Ser Ala Cys Val Tyr Xaa Cys Val
-10
                    -5
tgt atg tst gtg cgc gcg cat ctg tgt gtg tgc atg tgt gta tgt atg
                                                                       148
Cys Met Xaa Val Arg Ala His Leu Cys Val Cys Met Cys Val Cys Met
                                15
tgt gtg cat ctc tgt gtg tgc atg tgt gta tgt gtg tgt gca tct gtg
                                                                      196
Cys Val His Leu Cys Val Cys Met Cys Val Cys Val Cys Ala Ser Val
tgt gtg tgc atg tgt gca tgc gtg tgt atg tgt gtg tgc gtg cgt gca
                                                                      244
Cys Val Cys Met Cys Ala Cys Val Cys Met Cys Val Cys Val Arg Ala
                        45
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tct gtg tgt gtg c
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teegtgtata tggatttace tatteaggae attteatatg teetttggtg actggettet
                                                                       180
ttcactttgc acaatgtttt taaggttcat tcctgtcata gtgtgtgtca gtacgaaccc
                                                                       240
ctccttaacc atcta atg gtt atc acc tct aat agt tat ctc ata gcc aat
                                                                       291
                 Met Val Ile Thr Ser Asn Ser Tyr Leu Ile Ala Asn
                     -20
                                          -15
ctt gtt tta ttt ata tct atc gcc gcc ctc cgg g
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Leu Val Leu Phe Ile Ser Ile Ala Ala Leu Arg
                -5
<210> 321
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                                 Met Glu Glu Leu Asp Arg Lys Trp
                                      -50
aga gag aag gtc ctc cca gcg gca aag cta att aaa agg aga aac ctg
                                                                       102
Arg Glu Lys Val Leu Pro Ala Ala Lys Leu Ile Lys Arg Arg Asn Leu
            -40
                                -35
ttt tcc aca tgc act cct caa tat ggy aca cat gct gct ttc ttg tca
                                                                       150
Phe Ser Thr Cys Thr Pro Gln Tyr Gly Thr His Ala Ala Phe Leu Ser
        -25
                            -20
tta cat gcc.tca ctt gtc acc aaa gca ttt tca atc aat tcc tgg gag
                                                                       198
Leu His Ala Ser Leu Val Thr Lys Ala Phe Ser Ile Asn Ser Trp Glu
tgg
                                                                       201
Trp
<210> 322
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<211> 159

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<223> Von Heijne matrix
      score 5.5
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<400> 322
aacaaaggga cagaatggtc ccagggttcc ttcttcttcc ttccagttaa gagctcagag
                                                                       60
tggaagtggg ctgggg atg gtg tcg ggg gcc caa gct ccc agc tcc caa agg
                  Met Val Ser Gly Ala Gln Ala Pro Ser Ser Gln Arg
                  -25
ccc ctg ctt cta tgc cct ttg agc tca ggt agc ccc tgc ccc cgg gg
                                                                      159
Pro Leu Leu Cys Pro Leu Ser Ser Gly Ser Pro Cys Pro Arg
<210> 323
<211> 420
<212> DNA
<213> Homo sapiens
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<221> CDS
<222> 325..420
<221> sig_peptide
<222> 325..405
<223> Von Heijne matrix
      score 5.5
      seq SFLPSLLSSFLLS/LP
<221> misc feature
<222> 117
<223> n=a, g, c or t
catgcaggat agtaatacgt tagaatcaaa aataaggtta tacttagaaa atattgattt
                                                                       60
gcctttttga ttttgcatgt gtataatctg gctctgaaat cagtgacacg aagtganctt
                                                                      120
cgaaacaagc ctgagcaata gaagtagatg tggaaataac ttcggtttct caaggcaaat
                                                                      180
actttgatag gaacaaacaa ccgtttagat atagaagatg tgatacattc ctttaaaaag
                                                                      240
aatttgacct tatgtcattg taggcacacc tcatatttca attattcata tagtttttct
                                                                      300
tgagcaattg ctggtttaag aata atg tca tgt ctt ttg cgt gct tat atc
                                                                      351
                           Met Ser Cys Leu Leu Arg Ala Tyr Ile
                                   -25
att tgg ata ttt cct tcc ttc ctt cct tcc ctc ctt tct tcc ttc ctt
                                                                      399
Ile Trp Ile Phe Pro Ser Phe Leu Pro Ser Leu Leu Ser Ser Phe Leu
            -15
                                -10
ctt tcc ctc ccc cct tcc ggg
                                                                      420
Leu Ser Leu Pro Pro Ser Gly
<210> 324
<211> 210
<212> DNA
<213> Homo sapiens
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<220>
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<222> 9..209
<221> sig peptide
<222> 9..116
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    seq LHFVYCFLCCAEA/FL
<400> 324
ctccttat atg ttt cag tta ctg atc ctt tgt cag atg aat agt ttg aaa
                                                                        50
         Met Phe Gln Leu Leu Ile Leu Cys Gln Met Asn Ser Leu Lys
             -35
                                  -30
ata ttt tct ccc att ctt gga tgg tct ctt cat ttt gtt tat tgt ttc
                                                                        98
Ile Phe Ser Pro Ile Leu Gly Trp Ser Leu His Phe Val Tyr Cys Phe
                             -15
ctt tgc tgt gca gaa gcc ttt tta ctt gat atg atc cca ttt atg caa
                                                                       146
Leu Cys Cys Ala Glu Ala Phe Leu Leu Asp Met Ile Pro Phe Met Gln
                        1
ttt tac ttt ggt tac ctg tgc ttg tgg ggt att act tta aaa atc ttt
                                                                       194
Phe Tyr Phe Gly Tyr Leu Cys Leu Trp Gly Ile Thr Leu Lys Ile Phe
                15
gcc cag tcc aat tgg g
                                                                       210
Ala Gln Ser Asn Trp
            30
<210> 325
<211> 192
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<221> sig_peptide
<222> 31..174
<223> Von Heijne matrix
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      seq VCLRLHVLSAVQT/ER
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aggetgetge agttggegma tgaggegace atg gee ttg etg ggt aag ege tgt
                                                                       54
                                 Met Ala Leu Leu Gly Lys Arg Cys
gac gtc ccc acm aac ggc tgc gga ccc gac cgc wgg aam wac ggc gwy
Asp Val Pro Thr Asn Gly Cys Gly Pro Asp Arg Xaa Xaa Xaa Gly Xaa
-40
                    -35
                                         -30
aac ccg caa ara cga gat cat cac cag cmt mgt gtc tgc ctt aga ctc
                                                                       150
Asn Pro Gln Xaa Arg Asp His His Gln Xaa Xaa Val Cys Leu Arg Leu
                -20
                                    -15
cat gtg ctc agc gct gtc car act gaa cgc cga ggt gat ggg
                                                                      192
His Val Leu Ser Ala Val Gln Thr Glu Arg Arg Gly Asp Gly
                                1
<210> 326
<211> 181
<212> DNA
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<220>
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<222> 71..181
<221> sig_peptide
<222> 71..166 -
<223> Von Heijne matrix
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                                                                       60
agegegtegt atg egg eea gea eta agg tee tte tgg eac tee tet ggt
                                                                      109
           Met Arg Pro Ala Leu Arg Ser Phe Trp His Ser Ser Gly
                   -30
                                        -25
gga ccg ccc cca tcg gcc aca ctt gcc ctg ctc tcc agt gat tct gta
                                                                      157
Gly Pro Pro Pro Ser Ala Thr Leu Ala Leu Leu Ser Ser Asp Ser Val
                -15
get act ggc tee gta gte teg egg
                                                                      181
Ala Thr Gly Ser Val Val Ser Arg
<210> 327
<211> 185
<212> DNA
<213> Homo sapiens
<220>
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<222> 39..185
<221> sig peptide
<222> 39..116
<223> Von Heijne matrix
     score 5.5
     seq LFSGWLVWWGSRS/SQ
<221> misc_feature
<222> 143,145,175
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caaagacgca ctacttagta cagagaggtt ttgaatac atg ctc tqt qca tqc aaq
                                                                       56
                                          Met Leu Cys Ala Cys Lys
                                               -25
gca cgt ggg gtg atg ctg ctg ttc tca ggg tgg ttg gtt tgg tgg
                                                                      104
Ala Arg Gly Val Met Leu Leu Phe Ser Gly Trp Leu Val Trp Trp
                                         -10
ggc agt agg tcc tca cag two ctc aga atg cct gag agn tna gta agt
                                                                      152
Gly Ser Arg Ser Ser Gln Xaa Leu Arg Met Pro Glu Xaa Xaa Val Ser
ggg gag ggt cga agc gat cdv dng cca cat ggg
                                                                      185
Gly Glu Gly Arg Ser Asp Xaa Xaa Pro His Gly
        15
<210> 328
<211> 210
<212> DNA
<213> Homo sapiens
<220>
<221> CDS
<222> 57..209
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 <222> 57..182
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       score 5.5
       seq SLILPTSPSPAHS/GS
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 gacttaggts yaggcgactg cccagacaat gactggtccc gcataccgag cagagc atg
                                                                         59
 atc agc agc agt ctg agt gga aga gtg cct gtg atc tta ggg aac ctg
                                                                        107
 Ile Ser Ser Ser Leu Ser Gly Arg Val Pro Val Ile Leu Gly Asn Leu
     -40
                          -35
                                              -30
 atg ggc gtt gga gca gcg gtt cga cgc atg ggt ttc tct tta atc ctt
                                                                        155
 Met Gly Val Gly Ala Ala Val Arg Arg Met Gly Phe Ser Leu Ile Leu
                      -20
                                          -15
 ccg act tcc cca agc cca gcg cac tca ggt tcc gct cca agt gcg gga
                                                                        203
 Pro Thr Ser Pro Ser Pro Ala His Ser Gly Ser Ala Pro Ser Ala Gly
 ccc cgc g
                                                                        210
 Pro Arg
 <210> 329
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 <222> 149..316
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 <222> 149..286
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                                                                         60
 gatatttcag ttcctgattg taaatacctc ctaagcctga agcttctgtt actagccatt
                                                                        120
 gtgrgcttca gtktcttcak yckgcaaa atg ggc ata ata car kct att ctt
                                                                        172
                                 Met Gly Ile Ile Gln Xaa Ile Leu
                                     -45
 gcc aca tca agg gat tgt tat tcc ttt aaa aaa aca ata cca aag
                                                                        220
 Ala Thr Ser Arg Asp Cys Tyr Ser Phe Lys Lys Pro Ile Pro Lys
             -35
                                  -30
 aag cct aca atg ttg gcc tta gcc aaa att ctg ttg att tca acg ttg
                                                                        268
 Lys Pro Thr Met Leu Ala Leu Ala Lys Ile Leu Leu Ile Ser Thr Leu
         -20
                              -15
 ttt tat tca ctt cta tcg ggg agc cat gga aaa gra aat caa gac gtg
                                                                        316
 Phe Tyr Ser Leu Leu Ser Gly Ser His Gly Lys Xaa Asn Gln Asp Val
     -5
 gg
                                                                        318
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183 <222> 135..203 <223> Von Heijne matrix score 5.5 seq LPFVCLLLRNVYS/DL <400> 330 aacagtgtgt gagagttccc tttcctccac atcctcgcca gcatctgtta ttgcctgtct 60 ttttgatacg agccttttta acaggggtaa gatgatatct cattgtagtt ttgatttgca 120 ttctctgatg atca atg atg ttg agc acc ttt tca tat gcc tgt ttg cca 170 Met Met Leu Ser Thr Phe Ser Tyr Ala Cys Leu Pro -20 -15 ttt gta tgt ctt ctt ttg aga aat gtc tat tca gat ctt ttg ccc aat 218 Phe Val Cys Leu Leu Arg Asn Val Tyr Ser Asp Leu Leu Pro Asn cgg gg 223 Arg <210> 331 <211> 362 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 272..361 <221> sig_peptide <222> 272..343 <223> Von Heijne matrix score 5.5 seq LIVVLVCISLVII/DD <400> 331 aatggacacc taggttgctt ccatatctga gctattgtga ataatgctgc aatgaacatg 60 ggagtggaga catctcctaa gcatactgat ttcagttcct ttgggtatat acccagaagt 120 gggatcatgt ggtaatcttg tttttacttt tttgaggaac ctccatacca ttatccatga 180 tggctatagt aatttacatt cataccagca gtgcacaagg gtctcctttt ctgtatacac 240 ttgccaacac ttgttatctt tcattttttt g atg cta gcc att cta aca ggt 292 Met Leu Ala Ile Leu Thr Gly ggg agg tgg tat ctc ata gtg gtt tta gtt tgc att tcc ttg gtg att 340 Gly Arg Trp Tyr Leu Ile Val Val Leu Val Cys Ile Ser Leu Val Ile -15 362 att gat gat gag cac ggg g Ile Asp Asp Asp Glu His Gly 1 <210> 332 <211> 89 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 34..87 <221> sig_peptide <222> 34..75 <223> Von Heijne matrix score 5.5 seq LLPLGLKVLGLQA/RG

<400> 332

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cccagaccgg tettgaacte etggeetcaa etg atg ete etg eet etg ggt ete
                                                                         54
                                       Met Leu Leu Pro Leu Gly Leu
 aaa gtg ctg gga tta cag gcg aga ggc acc acg ct
                                                                         89
 Lys Val Leu Gly Leu Gln Ala Arg Gly Thr Thr
 <210> 333
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 <222> 255..398
 <221> sig_peptide
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ttcactgcaa ggcggcggca ggagaggttg tggtgctagt ttctctaagc catccagtgc
                                                                        60
catcetegte getgeagega cacaegetet egeegeegee atgaetgage agatgaecet
                                                                       120
tegtggcace etcaagggce acaacggetg ggtaacccag ategetacta cecegcagtt
                                                                       180
cccggacatg atceteceg cetetegagg tacggactaa gataagacca teateatgtg
                                                                       240
gaaactgacc aggg atg aga cca act atg gaa ttc cac agc gtg ctc tgc
                                                                       290
               Met Arg Pro Thr Met Glu Phe His Ser Val Leu Cys
                             -25
ggg gtc act ccc act ttg tta gtg atg tgg tta tct cct cag atg gcc
                                                                       338
Gly Val Thr Pro Thr Leu Leu Val Met Trp Leu Ser Pro Gln Met Ala
    -15
                         -10
agt tcg ccc tct cag gct cct ggg atg gaa ccc tgc gcc tct ggg atc
                                                                       386
Ser Ser Pro Ser Gln Ala Pro Gly Met Glu Pro Cys Ala Ser Gly Ile
                                     10
                                                         15
tca caa cgg gca a
                                                                       399
Ser Gln Arg Ala
<210> 334
<211> 188
<212> DNA
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<220>
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<222> 33..188
<221> sig_peptide
<222> 33..131
<223> Von Heijne matrix
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aatgaagggt actagaacac ctgcccatcc at atg gga aaa aaa aaa atc tgg
                                                                       53
                                    Met Gly Lys Lys Lys Ile Trp
                                                 -30
acc cct agc tca tat ccc atg ccc agt cat aaa cat gta tcc cta tgt
                                                                      101
Thr Pro Ser Ser Tyr Pro Met Pro Ser His Lys His Val Ser Leu Cys
                        -20
                                             -15
ctt cta acg gtt gca gtt tta gtt ctt aca ttt aag tct tta att cat
                                                                      149
```

.

Leu Leu Thr Val Ala Val Leu Val Leu Thr Phe Lys Ser Leu Ile His -5 -10 ttt gag tda att ttt gca tat gag ata ggg gtc cag ggg 188 Phe Glu Xaa Ile Phe Ala Tyr Glu Ile Gly Val Gln Gly <210> 335 <211> 115 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 23..115 <221> sig peptide <222> 23..94 <223> Von Heijne matrix score 5.5 seq CPSLLSPISPSQA/CP <400> 335 52 ccaatacaca teacteagtg go atg age eet gte etc tge tte eat ege tge Met Ser Pro Val Leu Cys Phe His Arg Cys -20 100 too tot coc toc ctc ago coc atc toc coa toc cag goo tgt cot Ser Cys Pro Ser Leu Leu Ser Pro Ile Ser Pro Ser Gln Ala Cys Pro -5 -10 115 gag ccc ctc ctt ggg Glu Pro Leu Leu Gly <210> 336 <211> 300 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 197..298 <221> sig_peptide <222> 197..268 <223> Von Heijne matrix score 5.5 seq IMFVCMCVCVC/VY <400> 336 60 catgettgtt gtaacgtgtc aaacaataca gaggtgtagg gaaaatacct agtgccaccc 120 tccactccaa aaccccatgt cgccagagat aaccatttat tcagacagtg agtatctatt aagtatctat tgctaggctt tggagatagc ataatgaaca aaatggatgt gctctctgcc 180 cttgtgattt ggacag atg ctt cag tta tct ttt tct gtg ttt ata ttg att 232 Met Leu Gln Leu Ser Phe Ser Val Phe Ile Leu Ile -20 280 atq ttt gta tgt atg tgc gtg tgt gtg tgt gtg tgt gtg tat cga ctg Met Phe Val Cys Met Cys Val Cys Val Cys Val Tyr Arg Leu -10 -5 300 ttt tct tcc tcc tcc ccg gg Phe Ser Ser Ser Pro

<210> 337 <211> 307

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      Met Lys Ser Thr Val Ser Ser Arg Glu Val Ala Thr Val Asp Lys
          -90
                              -85
 atg aaa aga cgc cat gca gaa tac tgt gca cag ggt ctc cag aga ttt
 Met Lys Arg Arg His Ala Glu Tyr Cys Ala Gln Gly Leu Gln Arg Phe
                         -70
                                              -65
 aaa gcc caa ctt tct caa gat acc ctt ccc cav cat cca cat ctg gag
                                                                        145
 Lys Ala Gln Leu Ser Gln Asp Thr Leu Pro Xaa His Pro His Leu Glu
                     -55
                                         -50
 awa gag aag ggg ctt gaa ggc ttg gag gaa aat gtg cct cta aag gga
Xaa Glu Lys Gly Leu Glu Gly Leu Glu Glu Asn Val Pro Leu Lys Gly
                                                                       193
                 -40
                                     -35
gag aaa cct gga gaa ggg ggt cca gag tct cct aag aag aga aga agg
                                                                       241
Glu Lys Pro Gly Glu Gly Gly Pro Glu Ser Pro Lys Lys Arg Arg Arg
             -25
                                 -20
gtg ctt ctc gga gcg ggc atc cca cca gta agc tca gct ccc agg aga
                                                                       289
Val Leu Leu Gly Ala Gly Ile Pro Pro Val Ser Ser Ala Pro Arg Arg
        -10
cag agc cag cag gca aca
                                                                       307
Gln Ser Gln Gln Ala Thr
                     10
<210> 338
<211> 123
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<222> 16..123
<221> sig_peptide
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      seq VHLFFFFFXETGS/RS
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                                                                        51
                 Met His Asn Ser Cys Arg Pro Val His Leu Phe Phe
                 -20
                                      -15
tit tit tit yet gag aca ggt tet egt tet aat yee tgg etg gag tse
                                                                       99
Phe Phe Phe Xaa Glu Thr Gly Ser Arg Ser Asn Xaa Trp Leu Glu Xaa
            ~ 5
agt ggt gcg atc ata gct aac tcc
                                                                      123
Ser Gly Ala Ile Ile Ala Asn Ser
    10
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<211> 451 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 318..449 <221> sig_peptide <222> 318..443 <223> Von Heijne matrix score 5.40000009536743 seq TFRLYLSLPVSQA/GP <221> misc_feature <222> 310..311,394 <223> n=a, g, c or t <400> 339 gtcacaaaag gagcactaag agcctgcttt actttcttcc tcagttgagt cgtggggaca' 60 gcttgaagga gccaacctca attgcagaga gcagccgtca ccccagctac cgctcagagc 120 ccagcttgga accagagagc ttccgttctc ctacctttgg caaaagtttt cacttcgatc 180 cactatccag tggctcacgc tcctccagcc tcaagtcagc ccagggcaca ggctttgagc 240 tgggccagtt gcaatccatt cgttcagagg gcaccacctc cacctcctaa taagagcctg 300 gccaaccagn nacgcaa atg gaa gcc tat ctt aat gac agc ttg ctc aca 350 Met Glu Ala Tyr Leu Asn Asp Ser Leu Leu Thr -40 -35 cet tea gae age eet gat tit gag tea gtg eag gea ggg eet gna gee 398 Pro Ser Asp Ser Pro Asp Phe Glu Ser Val Gln Ala Gly Pro Xaa Ala -25 -20 aga ccc acc ttt agg cta tac ctc tcc ctt cct gtc agc cag gct ggc 446 Arg Pro Thr Phe Arg Leu Tyr Leu Ser Leu Pro Val Ser Gln Ala Gly -15 -10 -5 cca gc 451 Pro <210> 340 <211> 304 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 94..303 <221> sig_peptide <222> 94..135 <223> Von Heijne matrix score 5.40000009536743 seq PALGPALLQGSLX/RV <221> misc feature <222> 244..245 <223> n=a, g, c or t <400> 340 gcgcagggga gaaacaaggc gccttggagt tcaggtgact cccacacggg tcatgctgtt 60

gteteetgat ceageeggee etgeeaggtg ace atg eet get etg gge eea get 114 Met Pro Ala Leu Gly Pro Ala -10 ett ete cag gge tet etg kge egv gtg ggt eet cae eet eea ges eet 162 WO 99/53051 PCT/IB99/00712

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Leu Leu Gln Gly Ser Leu Xaa Arg Val Gly Pro His Pro Pro Ala Pro
 tee ace aac tge att cae tee caa tgg cae gta tet gea gea esk gge
                                                                       210
 Ser Thr Asn Cys Ile His Ser Gln Trp His Val Ser Ala Ala Xaa Gly
 aag gga ccc cac ctc agg cac cct ctr sct ggg nns tac caa ctt cct
                                                                       258
 Lys Gly Pro His Leu Arg His Pro Leu Xaa Gly Xaa Tyr Gln Leu Pro
                                     35
 gtt cca gct gag ccc tgg gct gca gct gga ggc cac agt gtc cac c
                                                                       304
 Val Pro Ala Glu Pro Trp Ala Ala Ala Gly Gly His Ser Val His
 <210> 341
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 <221> CDS
 <222> 315..377
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<222> 315..371
<223> Von Heijne matrix
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       seq LCCSGCVPSLCCS/SY
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                                                                      . 60
gtcacattcg gttatctcta acgttggaaa acgatggagc taacacccat tatggagatt
                                                                       120
aamcvacttt tcatcaggtt tttaacttaa gtcgtgagga atacaacggt gaacacaaga
                                                                       180
ttcattttat tttcatcacc atgggacgta tcctgttgtt gagttctctg ggtcagacct
                                                                       240
ctgaagactt ctcagatgga tcctagtctc wrrgcttgcc ctgaaattac tcgctgctca
                                                                       300
gggagagagt tgaa atg gtt ggc atc ctc cca ctc tgt tgc tcc ggc tgt
                                                                       350
                Met Val Gly Ile Leu Pro Leu Cys Cys Ser Gly Cys
gtc ccc tcg ctc tgt tgt tcc agc tat gt
                                                                       379
Val Pro Ser Leu Cys Cys Ser Ser Tyr
<210> 342
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<222> 223..264
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      seq. AHSILLLASQAGC/LR
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                                                                       60
agcgtgggcc aggacagcgg gaggtaagtc gccaagaaaa gggttgggaa ragctcagaa
                                                                      120
tcggacggct aggaagaaat gaccaaaagg agcctgatag ccccctattc tgcacgctgt
                                                                      180
teetggaaac egeetttgea aagacagtga gagaaateta ac atg get cae tee
                                                                      234
                                                Met Ala His Ser
atc ttg ctt cta gcc tcg cag gcc ggc tgt ctt cgc tca ttc ctg ggc
                                                                      282
Ile Leu Leu Leu Ala Ser Gln Ala Gly Cys Leu Arg Ser Phe Leu Gly
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189 -10 -5 aat tgg g 289 Asn Trp <210> 343 <211> 169 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 78..167 <221> sig_peptide <222> 78..137 <223> Von Heijne matrix score 5.40000009536743 seq WVFLVAIFKGVHC/EG <400> 343 agetetggga gaggageeee egeeetggga tteecaggtg tttteatttg gtgateagea 60 ctgaacacag aagagtc atg acg gag ttt ggg ctg agc tgg gtt ttc ctt 110 Met Thr Glu Phe Gly Leu Ser Trp Val Phe Leu ~20 -15 gtt gct att ttt aaa ggt gtc cac tgt gaa ggt cma att ggt gga gtc 158 Val Ala Ile Phe Lys Gly Val His Cys Glu Gly Xaa Ile Gly Gly Val ggg ggg gcg gg 169 Gly Gly Ala <210> 344 <211> 112 <212> DNA <213> Homo sapiens ' <220> <221> CDS <222> 63..110 <221> sig_peptide <222> 63..104 <223> Von Heijne matrix score 5.40000009536743 seq NTVFLLLFFGCFF/FE <400> 344 tgtgttttct ctgtcccaaa ttaaatgcat tggggaagtt tataattaca ggaattccac 60 107 Met Asn Thr Val Phe Leu Leu Phe Phe Gly Cys Phe Phe Phe gag ac 112 Glu <210> 345 <211> 349 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 207..347

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gcb tgg tcc tgc tgc ttg tcc tca tcc tcg ttt att gcc gga aga Ala Trp Ser Cys Cys Leu Ser Ser Ser Phe Ile Ala Gly Arg -15 -5 1	281
agg agg ggc tgg act cag atg tgg ctg act cgt cca ttc tca cct cag Arg Arg Gly Trp Thr Gln Met Trp Leu Thr Arg Pro Phe Ser Pro Gln 5 10 15	329
gct tcc agc ccg tca gca tc Ala Ser Ser Pro Ser Ala 20	349
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att tct tca tat tcc cag aat gtg ttg tca aac ttt cac gat ggc tat Ile Ser Ser Tyr Ser Gln Asn Val Leu Ser Asn Phe His Asp Gly Tyr -25 -20 -15	104
ttt atg tta att ata ctt tct gcc att tta cta aat tct ttt att ggt Phe Met Leu Ile Ile Leu Ser Ala Ile Leu Leu Asn Ser Phe Ile Gly -10 -5	152
tgt gtc agc ttt tat cat tgc ttt tct tgg ggt tca ggg Cys Val Ser Phe Tyr His Cys Phe Ser Trp Gly Ser Gly 5 10 15	191
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gattcatcct cacgctaaac actcattcta cccaactgat tgagacagaa cagaagataa
                                                                       120
ctgaaacttc tctgccttcc cgctgcaaga agtgaatgag cgatccctct caactgactk
                                                                       180
raa atg ttt gcc tca ccc agg aga tgg agc tct ncg aag gcc ttc tct
                                                                       228
    Met Phe Ala Ser Pro Arg Arg Trp Ser Ser Xaa Lys Ala Phe Ser
                 -30
                                     -25
ggc cag cgg aca ctc cta tct gcc atc ctc agc atg cta tca ctc agc
                                                                       276
Gly Gln Arg Thr Leu Leu Ser Ala Ile Leu Ser Met Leu Ser Leu Ser
                                 -10
tto too aca aca too otg otc ago aac tac tgg ttt gtg ggc aca cag
                                                                       324
Phe Ser Thr Thr Ser Leu Leu Ser Asn Tyr Trp Phe Val Gly Thr Gln
aag gtg ccc aag ccc ctg tgc gag aaa ggt ctg gca gcc aag tgc ttt
                                                                       372
Lys Val Pro Lys Pro Leu Cys Glu Lys Gly Leu Ala Ala Lys Cys Phe
                    20
gac atg cca gtg tcc ctg gat gga gat acc aac aca tcc acc cag gag
                                                                      420
Asp Met Pro Val Ser Leu Asp Gly Asp Thr Asn Thr Ser Thr Gln Glu
                35
                                     40
gtg gta mma ta
                                                                       431
Val Val Xaa
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gtggagcagc tgcgcagtga gcagctgccc aagaaggaca ttatcaagtt tctgcaggaa
                                                                      120
cacggttcag attcggtacc agaggcgtag gggcggccgg gctggtgcgg ctgagggacg
                                                                      180
ceteacecee etggag atg cee.ata cat tee gta tte etc tgt gee eec gee
                                                                      232
                  Met Pro Ile His Ser Val Phe Leu Cys Ala Pro Ala
                      -15
ctc gtc ttc ccg cgg ccg gtg gcc tgg aag gcg gag agg ccc agc ttg
                                                                      280
Leu Val Phe Pro Arg Pro Val Ala Trp Lys Ala Glu Arg Pro Ser Leu
tgc ttt ggt gcc tcg ctc ccg cct ctc ggg cgt tct cta ctg ggg cag
                                                                      328
Cys Phe Gly Ala Ser Leu Pro Pro Leu Gly Arg Ser Leu Leu Gly Gln
ggg agc agc ttt att tct tgg ggc aca cag gct gca att gta gag tta
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Gly Ser Ser Phe Ile Ser Trp Gly Thr Gln Ala Ala Ile Val Glu Leu
                        35
kaa cct cat t
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Xaa Pro His
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                                                                        60
aattcaa atg gta tac gat gaa aaa tct ctc tcc tgt tcc cat acc cca
                                                                       109
        Met Val Tyr Asp Glu Lys Ser Leu Ser Cys Ser His Thr Pro
                -60
gcc acc cag ttc ctc tcc tgg gat gca tcc agt gtt tac agt ttc tta
                                                                       157
Ala Thr Gln Phe Leu Ser Trp Asp Ala Ser Ser Val Tyr Ser Phe Leu
            -45
                                 -40
tat atc ctc tca gca aga gtt aat gta gac gta dgc agm tac att cgt
                                                                      205
Tyr Ile Leu Ser Ala Arg Val Asn Val Asp Val Xaa Xaa Tyr Ile Arg
gtg tac ata ctt gcc tgt gtg ttt ttc ctc tca cac ccc ctt ttt aad
                                                                       253
Val Tyr Ile Leu Ala Cys Val Phe Phe Leu Ser His Pro Leu Phe Xaa
                        -10
sra cca aat ggt agt gta tat tgt cnm cgt cat tct ccc cct tac ctt
                                                                      301
Xaa Pro Asn Gly Ser Val Tyr Cys Xaa Arg His Ser Pro Pro Tyr Leu
1
                                     10
ttt tgc
                                                                      307
Phe Cys
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                                                                       58
ctg cct tta tca cct act aaa ttc cta aat gtg ttc ttg ggc ctg ttc
                                                                      106
Leu Pro Leu Ser Pro Thr Lys Phe Leu Asn Val Phe Leu Gly Leu Phe
-35
                    -30
                                         -25
etc tat tat ett caa ttg gta tgt etg ett att att tet ttg gtt ttg
                                                                      154
Leu Tyr Tyr Leu Gln Leu Val Cys Leu Leu Ile Ile Ser Leu Val Leu
ata tct ggg tta ggg g
                                                                      170
Ile Ser Gly Leu Gly
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ctgcattatt gactaccatt gaagaaatgc atttgctaag caaaaaaata ttcttcaatt
                                                                       120
agcttgaagt cttcatgcaa gtaaatta atg gac aag gtt gaa ctc cca cca
                                                                       172
                               Met Asp Lys Val Glu Leu Pro Pro
                                                -25
ect gat ett gga eca agt tet gea eta aat eag aca ete atg ttg etg
                                                                       220
Pro Asp Leu Gly Pro Ser Ser Ala Leu Asn Gln Thr Leu Met Leu Leu
    -20
                         -15
cgt gaa gtt tta gca tct cac gat tct tca gtk gta cca tta gat gct
                                                                       268
Arg Glu Val Leu Ala Ser His Asp Ser Ser Val Val Pro Leu Asp Ala
cgt caa gct gat ttt gtg cag ggg g
                                                                       293
Arg Gln Ala Asp Phe Val Gln Gly
            15
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acaggctgtg ggagggttat tagttggtct aatttcaata mtgttccttt cyccagggaa
                                                                       120
ttgnraggcc caaggagagg gagagag atg ggg gga aca gct ggt tgg agc agt
                                                                       174
                              Met Gly Gly Thr Ala Gly Trp Ser Ser
                                       -30
cag aac aca cac aac att kga gta cac cat ctt gtg tgg ctg tgg ttc
                                                                      222
Gln Asn Thr His Asn Ile Xaa Val His His Leu Val Trp Leu Trp Phe
            -20
                                -15
gtg gtc ccc caa aca att aca atg ata aca cca aag atc act gaa cac
                                                                      270
Val Val Pro Gln Thr Ile Thr Met Ile Thr Pro Lys Ile Thr Glu His
aga cca sta ata aca gat atr dtr ata atg aya aca ttt gaa awa ttg
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Arg Pro Xaa Ile Thr Asp Xaa Xaa Ile Met Xaa Thr Phe Glu Xaa Leu 20 gga gaa tta ccc a 331 Gly Glu Leu Pro <210> 355 <211> 93 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 2..91 <221> sig peptide <222> 2..55 <223> Von Heijne matrix score 5.30000019073486 seq ALYLCVCVCVCLI/AR t atg tgt ctv agt gta gct ttg tat tta tgt gtg tgt gtg tgt gta tgt Met Cys Leu Ser Val Ala Leu Tyr Leu Cys Val Cys Val Cys -10 ctg att gca cgg gtg tac ttt tgt att tat gtg tgt gtg tgg tt 93 Leu Ile Ala Arg Val Tyr Phe Cys Ile Tyr Val Cys Val Trp <210> 356 <211> 178 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 92..178 <221> sig peptide <222> 92..133 <223> Von Heijne matrix score 5.30000019073486 seq LHLLFGLFPVLWM/FL <400> 356 tgaccettgt ccagtetttt ccaggaaaaa catgeeetca agatgttttt ctatettgag 60 gaaatgatgg aaatgagata gttccaaggg t atg ctt cac ctt ctt ttt ggc 112 Met Leu His Leu Leu Phe Gly tta ttt cct gtt ctt tgg atg ttt cta gtg tat ttc ttt ctt tct 160 Leu Phe Pro Val Leu Trp Met Phe Leu Val Tyr Phe Phe Leu Ser Ser ttt ttt ttt ttt ttt 178 Phe Phe Phe Phe Phe <210> 357 <211> 107 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 40..105

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                                         Met Tyr Val Cys Xaa
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                                                                   102
Cys Val Tyr Leu Phe Cys Ala Cys Met Cys Val Cys Ala Phe Phe
           -10
ttt tt
                                                                   107
Phe
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                                                                    55
                                              Met Lys Xaa Asn
                                                  -35
aac ctc cgg cga cag agc ccc gct ctc agg cac tgc tgg aga mcc gag
                                                                   103
Asn Leu Arg Arg Gln Ser Pro Ala Leu Arg His Cys Trp Arg Xaa Glu
       -30
                           -25
                                              -20
acc gac ttc ttt ctc ttt acc ctc att ggc gct tct ctc ctg cag tcc
                                                                   151
Thr Asp Phe Phe Leu Phe Thr Leu Ile Gly Ala Ser Leu Leu Gln Ser
                       -10
gcc tct ggg ccc tgc cgc att tct tsa smc tta aag tgg cat tct aaa
                                                                   199
Ala Ser Gly Pro Cys Arg Ile Ser Xaa Xaa Leu Lys Trp His Ser Lys
ggc act tta a
                                                                   209
Gly Thr Leu
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197

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198

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Leu Glu Arg Gly Asp Glu Pro Trp Val Leu Asp Val Gln Gly Thr Ser
ggg aaa gag cac ctg aag aag tca aca gcc cag ctc ttg gga cca gaa
                                                                       440
Gly Lys Glu His Leu Lys Lys Ser Thr Ala Gln Leu Leu Gly Pro Glu
ctg aag tac aag gag ttg ay
                                                                       460
Leu Lys Tyr Lys Glu Leu
        90
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gtacgaggcg gtgcgggaag tcctgcacgg gaaccagcgc aasgccgcaa gttcctgqaq
                                                                      120
acggtggagt tgcaggatca gcttgaagaa ct atg atc ccc aga agg aca agc
                                                                      173
                                    Met Ile Pro Arg Arg Thr Ser
gct tct cgg gca ccg tca gtc ccc caa aac gca ggc tta agt cca ctc
                                                                      221
Ala Ser Arg Ala Pro Ser Val Pro Gln Asn Ala Gly Leu Ser Pro Leu
-30
                    -25
                                         -20
ccc gcc cta agt tct ctg tgt gtg tcc tgg ggg acc agc agc act gtg
                                                                       269
Pro Ala Leu Ser Ser Leu Cys Val Ser Trp Gly Thr Ser Ser Thr Val
                -10
acg agg cta agg ccg tgg ata tcc ccc aca tgg aca tcg agg gcg cgg g
                                                                      318
Thr Arg Leu Arg Pro Trp Ile Ser Pro Thr Trp Thr Ser Arg Ala Arg
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cctttatcag atacatgttt tgcaaatgtt ttctaccatt ctctgtctdh tctttctctt
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aatactttca cagtttttca tagcagaaat ttataaatta atgaagccca ctttatactt	180 230
ttatttcttt t atg gtt tgc atc ttt tgt ttc tta act tcg aaa gct ttt Met Val Cys Ile Phe Cys Phe Leu Thr Ser Lys Ala Phe	230
-10 -5	
cct aac cct aga tca cag gat ttt ctc tta gat ttc tct agg cat tnt	278
Pro Asn Pro Arg Ser Gln Asp Phe Leu Leu Asp Phe Ser Arg His Xaa	
1 5 10 15	
ata ggt tta ggt ttc aca ttt agg tcc gca atg cat ttt gaa aac ttc	326
Ile Gly Leu Gly Phe Thr Phe Arg Ser Ala Met His Phe Glu Asn Phe 20 25 30	
cgt ctg waa ggt ttg ggt caa gat tcc ctt tgt c	360
Arg Leu Xaa Gly Leu Gly Gln Asp Ser Leu Cys	300
35 40	
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beq or do viscor many on	
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-111	
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actttaactt cctggagctc taatttctcc ttctcaggta gaagaatgcc attcactccc aagtggtgag nmncaagcag ccagtggtag gaagggtcat caagtcagtt gtcagaaacc	.60 120
tcactk atg tca ctg twt ahg cta tgt gac cct gac cta gtt cct tgc Met Ser Leu Xaa Xaa Leu Cys Asp Pro Asp Leu Val Pro Cys -20 -15 -10	168
cct ctc ttg atc tca gtt gct tta tct gta aaa ttt cac att tkt cag Pro Leu Leu Ile Ser Val Ala Leu Ser Val Lys Phe His Ile Xaa Gln -5	216
caa gtc aac ctt cca tgt tcc tct ca Gln Val Asn Leu Pro Cys Ser Ser 10 15	242
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aaa aga aac ccc aaa cct gtt aca gtc cct gct ttt ctg csc cct tgc Lys Arg Asn Pro Lys Pro Val Thr Val Pro Ala Phe Leu Xaa Pro Cys -25 -20 -15 -10	96
ttg act tct ttc tct tgt kct gga gca tct ttc tct ctk ttw ggt gdg Leu Thr Ser Phe Ser Cys Xaa Gly Ala Ser Phe Ser Leu Xaa Gly Xaa -5 5	144
aga agg ggt tgg caa cat ggc agc tgc tgc tcc acc att ccc tta ttt Arg Arg Gly Trp Gln His Gly Ser Cys Cys Ser Thr Ile Pro Leu Phe 10 15 20	192
csa act cta aat tcc ctt ggg cag gga ctc att ggc cca gcc tac ata Xaa Thr Leu Asn Ser Leu Gly Gln Gly Leu Ile Gly Pro Ala Tyr Ile 25 30 35	240
ggt gcd gg Gly Ala 40	248
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<222> 36
<223> n=a, g, c or t
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aaagtagagg tactcaaatg actttcaact gataaacaca gatgaacaaa atgtatgtcc
                                                                       120
aaacagtaga atattattca gctataaaaa agaacagagt acacttagca aactaagaat
                                                                       180
agaaggaact tcctcaatct gataaaggac atccatgaaa aacccaccac taatgtcata
                                                                       240
cttaatcatg aaaaaccgaa tgcttttctc ctaagatagg aaaaagacaa gt atg tct
                                                                       298
act cat gcc atc tct att cta ctt tgt att ggt gct tct agc cag ggc
                                                                       346
Thr His Ala Ile Ser Ile Leu Leu Cys Ile Gly Ala Ser Ser Gln Gly
agg gg
                                                                       351
Arg
<210> 367
<211> 208
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<221> sig peptide
<222> 7..99
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gtctcg atg gag gag caa gaa acg gaa gag gtc ggg ggg aga agc agc
       Met Glu Glu Glu Thr Glu Glu Val Gly Gly Arg Ser Ser
           -30
                                -25
egg aaa aat gea gee ace gte aac gee gee tee etg eea eeg tge tte
                                                                        96
Arg Lys Asn Ala Ala Thr Val Asn Ala Ala Ser Leu Pro Pro Cys Phe
                             -10
ggg gta aaa age tge egt tge egt egg tge agt tge egt ege tge ete
                                                                       144
Gly Val Lys Ser Cys Arg Cys Arg Arg Cys Ser Cys Arg Arg Cys Leu
cta tac ttc tct tgg cct cgg gga agg att tcc cca ccg gtg gga caa
                                                                       192
Leu Tyr Phe Ser Trp Pro Arg Gly Arg Ile Ser Pro Pro Val Gly Gln
                                     25
                                                         30
tgt gcg ggg agg gga t
                                                                       208
Cys Ala Gly Arg Gly
            35
<210> 368
<211> 446
<212> DNA
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202

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<223> Von Heijne matrix

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<211> 132
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<213> Homo sapiens
<220>
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<221> sig_peptide
<222> 39..77
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      seq MLLAVSLSLVSNC/NF
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atcttagagg aaagtctttc agtttttccc cattcagt atg tta tta gct gtg agc
                                                                        56
                                           Met Leu Leu Ala Val Ser
                                                       -10
ctg tcc ctt gtc tct aat tgt aac ttt gta ctc act gac caa ctt ttc
                                                                       104
Leu Ser Leu Val Ser Asn Cys Asn Phe Val Leu Thr Asp Gln Leu Phe
        -5
cct gcc cct gcs tcc ctc atc ccc gaa g
                                                                       132
Pro Ala Pro Ala Ser Leu Ile Pro Glu
<210> 371
<211> 127
<212> DNA
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<220>
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<222> 4..126
<221> sig_peptide
<222> 4..90
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      seq TGVFLFSIIGSFG/FP
<400> 371
tga atg aac caa gat ttc aac cca gaa att gag gct tca cca caa gtg
                                                                       48
    Met Asn Gln Asp Phe Asn Pro Glu Ile Glu Ala Ser Pro Gln Val-
                    -25
                                        -20
aag act ggg gtt ttc ttg ttt tca att att ggg agt ttt gga ttt cca
                                                                       96
Lys Thr Gly Val Phe Leu Phe Ser Ile Ile Gly Ser Phe Gly Phe Pro
                -10
gga atg tgc aat tgt aaa aac cca gcc cgg g
                                                                       127
Gly Met Cys Asn Cys Lys Asn Pro Ala Arg
<210> 372
<211> 196
<212> DNA
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<222> 125..196
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score 5.19999980926514 seq IVSSLFSWLLSLT/SV

<221> misc_feature <222> 119 <223> n=a, g, c or t

<400> 372

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cccatcttaa gcccatggca acccctgatc tttttactgt ctccatcgtt ttgccttbnc
caga atg cca tgt agt tgg agt cat ata gta agt agc ctt ttc agt tgg
Met Pro Cys Ser Trp Ser His Ile Val Ser Ser Leu Phe Ser Trp
-20
-15
-10

ctt ctt tca ctt acc agt gtg ccc ggg
Leu Leu Ser Leu Thr Ser Val Pro Gly
-5

<210> 373 <211> 148 <212> DNA <213> Homo sapiens

<220> <221> CDS <222> 56..148

<400> 373

acttectica cacccaggac geagggtgee getgeeggee acagaaacce caaga atg Met

ttt ttc ttt ggc tat tea gag gac atc tat tgt gtg tea ggc ect gtg

Phe Phe Phe Gly Tyr Ser Glu Asp Ile Tyr Cys Val Ser Gly Pro Val

-25 -20 -15

ctg age tgt tgt tgc etg aca gea gga aga geg egg ete tgg 148

Leu Ser Cys Cys Cys Leu Thr Ala Gly Arg Ala Arg Leu Trp

<210> 374 <211> 200 <212> DNA <213> Homo sapiens

<220>
<221> CDS
<222> 26..199

<221> sig_peptide
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<223> Von Heijne matrix
score 5.19999980926514
seq AALICPWSSQVPS/SP

<400> 374

Ctagggagga ctcaatgctc tttgt atg cct tat gca gcg ctg atc tgt ccc 52

Met Pro Tyr Ala Ala Leu Ile Cys Pro

-15

tgg agt tcc cag gtt ccc agc tcc ccc gca agc ctt gaa gcc tcc

100

205

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Trp Ser Ser Gln Val Pro Ser Ser Pro Pro Ala Ser Leu Glu Ala Ser
        -5
                            1
age aac gtc tat etc eag gag age agg gea gee tat gea agt gtt eeg
                                                                      148
Ser Asn Val Tyr Leu Gln Glu Ser Arg Ala Ala Tyr Ala Ser Val Pro
                    15
gca gga cca gaa gtg gcc act caa cac acg tcc tca cca qtc acc cct
                                                                      196
Ala Gly Pro Glu Val Ala Thr Gln His Thr Ser Ser Pro Val Thr Pro
                30
                                                                      200
Met
<210> 375
<211> 112
<212> DNA
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<222> 52..111
<221> sig_peptide
<222> 52..105
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      seq LTYSLAFLLFIKA/GT
aataaccctt tcacagcact tgcctgtttt taatgaatct aattattcac a atg caa
                                                                       57 ·
                                                         Met Gln
ctt tta tat tta aca tac tct tta gct ttc ctg cta ttt atc aag gct
                                                                      105
Leu Leu Tyr Leu Thr Tyr Ser Leu Ala Phe Leu Leu Phe Ile Lys Ala
   -15
                        -10
ggc acc g
                                                                      112
Gly Thr
<210> 376
<211> 146
<212> DNA
<213> Homo sapiens
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<221> CDS
<222> 74..145
<221> sig_peptide
<222> 74..133
<223> Von Heijne matrix
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      seq AAAVTSSAAPSRA/RQ
<400> 376
ggctggagcg cgcgcctcct agcggascgg ggcaattgga aggccgcgcc tcaggaaaac
                                                                     . 60
aggatggtag tga atg gca ccg agc cgc ccc agg gct gcc gcc gtc acc
                                                                     109
               Met Ala Pro Ser Arg Pro Arg Ala Ala Ala Val Thr
               -20
                                   -15
tcc tcg gcg gct ccg agt cgt gcg agg cag ggg gcc c
                                                                     146
Ser Ser Ala Ala Pro Ser Arg Ala Arg Gln Gly Ala
<210> 377
<211> 389
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<212> DNA

<213> Homo sapiens

<220> <221> CDS

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<221> sig peptide
<222> 218..343
<223> Von Heijne matrix
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<221> misc_feature
<222> 139
<223> n=a, g, c or t
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ctcgctcatc ggtgttcgtg ggctttgtcg gtccgtgcct cgtctctccc tggaaaggga
                                                                      120
gggaggette gacgtegrnr aggragmmge tgeegegtta gtteegaget tgaagteact
                                                                      180
aggacttete teaaacttgt gtgetgagga gacteag atg ttg gee tea get eet
                                                                      235
                                          Met Leu Ala Ser Ala Pro
                                                  -40
agg ctg aac tca gca gat cgg ccc atg aaa act tct gta ttg aga caa
                                                                      283
Arg Leu Asn Ser Ala Asp Arg Pro Met Lys Thr Ser Val Leu Arg Gln
agg aag gga tot gto aga aag caa cac ttg tta tot tgg got tdg cag
                                                                      331
Arg Lys Gly Ser Val Arg Lys Gln His Leu Leu Ser Trp Ala Xaa Gln
                    -15
                                        -10
yaa ggh aga kga cag gta gtg gag atc ctg caa tct gaa aag cag act
                                                                      379
Xaa Gly Arg Xaa Gln Val Val Glu Ile Leu Gln Ser Glu Lys Gln Thr
                                5
daa rgt gac g
                                                                      389
Xaa Xaa Asp
        15
<210> 378
<211> 143
<212> DNA
<213> Homo sapiens
<220>
<221> CDS
<222> 2..142
<221> sig_peptide
<222> 2..115
<223> Von Heijne matrix
      score 5.19999980926514
      seq LHGSLDAVSQAQG/RP
<400> 378
a atg tac ccc cta ggc agg gga gag cag ggc cct gct gca ccc aag tcc
                                                                       49
 Met Tyr Pro Leu Gly Arg Gly Glu Gln Gly Pro Ala Ala Pro Lys Ser
              -35
                                  -30
tgg ttg ctc ctc ccc acc aca ctg gcc ctc cat gga agc ctt gat gca
                                                                       97
Trp Leu Leu Pro Thr Thr Leu Ala Leu His Gly Ser Leu Asp Ala
        -20
                            -15
                                                 -10
gtg agc cag gcc caa gga cgc ccc ggc cac cct gac gca ccc ccc a
                                                                      143
Val Ser Gln Ala Gln Gly Arg Pro Gly His Pro Asp Ala Pro Pro
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<221> CDS

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207
<210> 379
<211> 261
<212> DNA
<213> Homo sapiens
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<221> CDS
<222> 198..260
<221> sig peptide
<222> 198..245
<223> Von Heijne matrix
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attagtttaa ccattgtgga agatgatatg gcaattccac aaagacctaa agtcagraat
                                                                       120
tmcmattcaa cccagtaatc ccattactgg gtatatactc aaaggaatat aaattgttgt
                                                                       180
gttacaaaga cacatgc atg cgt gtg ttc att gca gca ctg ttc aca ata
                                                                       230
                   Met Arg Val Phe Ile Ala Ala Leu Phe Thr Ile
                       -15
gca gag aca tgg aat caa ccc aaa tgc cca g
                                                                       261
Ala Glu Thr Trp Asn Gln Pro Lys Cys Pro
<210> 380
<211> 228
<212> DNA
<213> Homo sapiens
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<221> CDS
<222> 63..227
<221> sig_peptide
<222> 63..152
<223> Von Heijne matrix
      score 5.19999980926514
      seq LCFLSVHFRLRWG/DS
<400> 380
                                                                        60
gggacgtggg aaaatgacta cgcgtcactc gtgatgtcgc gcatccgata ggcccttttc
ag atg gca aaa ggc ctg agg gtg aat ctg ggc gag ctg gtt gag tcc
                                                                       107
   Met Ala Lys Gly Leu Arg Val Asn Leu Gly Glu Leu Val Glu Ser
                       -25
   -30
atg cgt ttg tgc ttc ctc tca gtc cac ttt cgc tta cga tgg ggc gac
                                                                       155
Met Arg Leu Cys Phe Leu Ser Val His Phe Arg Leu Arg Trp Gly Asp
-15
                     -10
                                         -5
                                                                       203
tot tgt cca tcg tca cct cac cgg gaa act ttt cct gcc ggg cca gtt
Ser Cys Pro Ser Ser Pro His Arg Glu Thr Phe Pro Ala Gly Pro Val
                                 10
                                                                       228
aat ggt ccc ctg tac cac ccc cgg g
Asn Gly Pro Leu Tyr His Pro Arg
        20
                             25
<210> 381
<211> 300
<212> DNA
<213> Homo sapiens
<220>
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<222> 39..299

<221> sig_peptide

<222> 39..89

<223> Von Heijne matrix
 score 5.09999990463257
 seq QLLVLFGSQTGTA/QD

<400> 381

agtttttagt ctcagaccag accaccgggc gcgccccg atg ccg agc ccg cag ctt 56

Met Pro Ser Pro Gln Leu

-15

145

ctg gtg ctc ttc ggc agc cag aca ggc acg gct cag gat gtg tcg gag 104 Leu Val Leu Phe Gly Ser Gln Thr Gly Thr Ala Gln Asp Val Ser Glu -10 -5 1 5

aga ctg ggt cgc gag gcc cgg ggc cgg ctt ggc tgc cgg gtg cag
Arg Leu Gly Arg Glu Ala Arg Gly Arg Arg Leu Gly Cys Arg Val Gln

gcc ctg gac tcc tac ccg gtg gtg aat ctg att aac gag ccc ctg gtg
Ala Leu Asp Ser Tyr Pro Val Val Asn Leu Ile Asn Glu Pro Leu Val
25
30
35

ata ttt gtt tgt gca act ayw ggc caa gga gac ccc cct gac aac atg

1le Phe Val Cys Ala Thr Xaa Gly Gln Gly Asp Pro Pro Asp Asn Met

40

45

50

aag aac ttc tgg agg ttt ata ttc cgg aag aac ctg ccc tcc acc gcc

Lys Asn Phe Trp Arg Phe Ile Phe Arg Lys Asn Leu Pro Ser Thr Ala

55 60 65

cgg g Arg

<210> 382

70

<211> 151

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> 8..151

<221> sig_peptide

<222> 8..130

<223> Von Heijne matrix
score 5.09999990463257
seq SFLFLACIFQGXS/XX

<400> 382

atacata atg tct tcc att ttg ggt gtc tca tcc tca tgg tgg tat tta

Met Ser Ser Ile Leu Gly Val Ser Ser Ser Trp Trp Tyr Leu

-40

-35

tat tat ggc tat tgt ata ttt gtt aaa aag tgc tct ttt tgc agt ttc

97

Tyr Tyr Gly Tyr Cys Ile Phe Val Lys Cys Ser Phe Cys Ser Phe
-25
-20
-15

ctg ttc ctt gcc tgt att ttt caa ggc tkt tck ckt kat wca aac aca Leu Phe Leu Ala Cys Ile Phe Gln Gly Xaa Ser Xaa Xaa Xaa Asn Thr -10

caa agc 151 Gln Ser

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ggġ c Gly L																163
ccg t Pro C	ys :															211
act a Thr A 10	ga	ttg					ttc							gg		255
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gtgta	gt	atg	agc Ser	wkr	wtt	agm	agg	ttg Leu	stt	aga		ctg	ctc Leu	tcc	cag	169
rtg a Xaa A																217
tct a		ttt					tct									265
gtg c Val F																313
atg c Met I																361
aat a Asn T																409
			+a+	kar	att	tca	aat	ata	ana	cta	cta	cta	tca	cat	са	456

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Leu Xaa Ser Ser Xaa Val Ser Asn Val Arg Leu Leu Leu Ser His
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atg cct cat cca ctg gct acc tct gcg ttt ctg cgt tcc gcc ttt cct
                                                                        48
Met Pro His Pro Leu Ala Thr Ser Ala Phe Leu Arg Ser Ala Phe Pro
                        -20
ttt gtt tgt ctc acg ttt tgc gtg gga ggc ggt ccc ggg att tca ggg
                                                                        96
Phe Val Cys Leu Thr Phe Cys Val Gly Gly Gly Pro Gly Ile Ser Gly
                    -5
gtc tac cgg ctc ctt atg gcg aat gca acc cga aga gag agt gag gta
                                                                       144
Val Tyr Arg Leu Leu Met Ala Asn Ala Thr Arg Arg Glu Ser Glu Val
                                15
ago etc ege ggg ttg gge agg gac gga gag ggg gee ege geg act eea g
Ser Leu Arg Gly Leu Gly Arg Asp Gly Glu Gly Ala Arg Ala Thr Pro
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<221> sig_peptide
<222> 199..267
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tgtttatagg ttttaactct tatggttaga atggttgtga gtcatacgwg tgtcagacct
                                                                       60
ctgctaattt cctcaggaca cattcccaga agtggaatta ccaagtcaaa gagcataaat
                                                                      120
actttagaga tacatgataa attgtgccag ctacctttcc aaaagagttg tactagttga
                                                                      180
ggtttctgcc agcagtat atg aca gtt ggg ctc cat att tta aga gat tca
                                                                      231
                    Met Thr Val Gly Leu His Ile Leu Arg Asp Ser
                                -20
cta atg gtg ttt ctc aac ctt ttt ttt tta aac tgt gac cca cac agg
                                                                      279
Leu Met Val Phe Leu Asn Leu Phe Phe Leu Asn Cys Asp Pro His Arg
        -10
                            -5
99
                                                                      281
<210> 387
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<221> <222> <223>	5. Vo	.67 n He ore	ijne 5.09	mat 9999	rix 99046 HAYP/		,									•	
<400> cacc	atg	gta	Arg					Pro				_	. Ser		ctg Leu		49
ctc c Leu H						_				_		_	_				97
agg c Arg F				9 9			,									:	111
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<400>							**			••		. b. m. a. b				-	60
cgggd									tc a	etg g		199 S	gct g	gct (113
tgg g Trp V										tgt	ttt						161
ggt g Gly A					tgc					999							209
gtt d Val I				gaa				cag					acc				257
cac o	_	gtt															305
gga t Gly I	ttg					acc					atg						353
cac o					tct		•										374

<213> Homo sapiens

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<222> 184..300
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cogttatgtg ttcagctcaa ttagattaat taccttcctc accaggagtc acaatgcttt
                                                                        60
gcagtttatc tgcggtaact aaatgttagt tttgtaagta aaaggtactg ttattgacct
                                                                       120
cgaaagggct atagttcctt tgaacttaca gagaagagtt ccaaacaact atttctaacc
                                                                       180
aag atg gaa tat ggg tca gca aaa ttg tct tca ggt aga gtt ttc tac
                                                                       228
   Met Glu Tyr Gly Ser Ala Lys Leu Ser Ser Gly Arg Val Phe Tyr
                    -35
                                        -30
ttg cca aga gac ttt ggc att gag agg aga gtt ctt gtt tgt ttt ttt
                                                                       276
Leu Pro Arg Asp Phe Gly Ile Glu Arg Arg Val Leu Val Cys Phe Phe
                -20
                                    -15
aac tot gta toa ttt otg ttt ggt gto tot ara aaa aaa too gra caa
Asn Ser Val Ser Phe Leu Phe Gly Val Ser Xaa Lys Lys Ser Xaa Gln
tgg g
                                                                       328
Trp
<210> 392
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<221> sig_peptide
<222> 252..290
<223> Von Heijne matrix
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      seq MLSGLVLNSWALA/YQ
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tgaccttgta gcagttatct ttgttaaact ccttcatttc ttatttaaa taattaatta
                                                                        60
attaatttag agacagggtc tcactatgtc acccaggctg tagtgcagtg gtgcaatcat
                                                                       120
ggeteactgt ageettgace teccaggete aageaatett cetaceteag ceteteagge
                                                                       180
agetgggaet acagacecae ageactaege etgaettatg attttatttt ttgtggagae
                                                                      240
agggtettae t atg ttg tet ggg ett gte tta aac tet tgg gee tta gee
                                                                       290
             Met Leu Ser Gly Leu Val Leu Asn Ser Trp Ala Leu Ala
                         -10
tac caa cta gct g
                                                                       303
Tyr Gln Leu Ala
<210> 393
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<221> misc feature
<222> 265
<223> n=a, g, c or t
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tgagegeteg cegtettttg geggeagegg egaegegagg geteeeggee geeegegtee
                                                                   120
gctgggaatc tagcttctcc argamytgtg gtcgccccgt ccgctgtggc gggaaagcgg
                                                                   180
tececagaac egaceacace gtggeaagag gacecagaac eegaggaega aaacttgtat
                                                                   240
gagaagaasc cagactccca tggknatgac aaggaccccg ttttggacgt ctggaac
                                                                   297
atg cga ctt gtc ttc ttc ktw ggc gks tcc atc atc ctg gtc ctt ggc
                                                                   345
Met Arg Leu Val Phe Phe Xaa Gly Xaa Ser Ile Ile Leu Val Leu Gly
                       -10
   -15
age ace ttt gkg gee tat etg
                                                                   366
Ser Thr Phe Xaa Ala Tyr Leu
<210> 394
<211> 126
<212> DNA
<213> Homo sapiens
<220>
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<222> 21..125
<221> sig_peptide
<222> 21..68
<223> Von Heijne matrix
     score 5
     seq SDFFLLFVSLSLS/PF
<400> 394
agettggeat ataggeteaa atg tta tea tea gat ttt ttt ete ete ttt gte
                                                                    53
                     Met Leu Ser Ser Asp Phe Phe Leu Leu Phe Val
                         -15
                                             -10
101
Ser Leu Ser Leu Ser Pro Phe Pro Phe Leu Phe Pro Pro Leu Phe
tcc tgc ttt ctc tta ccc acc cgg g
                                                                   126
Ser Cys Phe Leu Leu Pro Thr Arg
           15
<210> 395
<211> 329
<212> DNA
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<222> 154..327
<221> sig peptide
<222> 154..195
<223> Von Heijne matrix
     score 5
     seq FIAALFTVAKIWN/QP
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acaataaaac tcccatatga tccagcaatc ctaccactgr atatttatcc aaaggaaagg	120
aagtoggtat atttaacagg catotgoaco ooo atg ttt att goa goa ota tto	174
Met Phe Ile Ala Ala Leu Phe	
-10 ·	
aca gta gcc aag ata tgg aat caa cct aaa tgt cca tca acg gat gaa	222
Thr Val Ala Lys Ile Trp Asn Gln Pro Lys Cys Pro Ser Thr Asp Glu	
-5 1 5	
tgg ata aat aaa atg tgg tac ata tac aca atg gag tac tat cca gac	270
Trp Ile Asn Lys Met Trp Tyr Ile Tyr Thr Met Glu Tyr Tyr Pro Asp	
10 15 20 25	
ata aaa aag aat gga att ctg aca ttt aag gca aca agg atg aac cgg	318
Ile Lys Lys Asn Gly Ile Leu Thr Phe Lys Ala Thr Arg Met Asn Arg	
30 35 40	
aag aca tta tg	329
Lys Thr Leu	
•	
<210> 396	
<211> 99	
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· · · · · · · · · · · · · · · · · · ·	
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<222> 549	
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score 5	
seg VCGCLCVWMCVCG/XV	
bed vecebernieved/hv	
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(223) N=a, g, c or c	
·	
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gtat atg tgt gtg tgt ggg tgt tta tgt gtg tgg atg tgt gtg tgt ggn	49
Met Cys Val Cys Gly Cys Leu Cys Val Trp Met Cys Val Cys Gly	43
	07
with gig tigt ata tac ata tigm gig tat gig tigt aca tigt gig agg gigg	97
Xaa Val Cys Ile Tyr Ile Xaa Val Tyr Val Cys Thr Cys Val Arg Gly	
1 5 10 15	
ga	99
<210> 397	
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score 5	
TO THE EVERY VOICE OF THE	

<222> 10..120

216 <221> misc_feature <222> 284..285 <223> n=a, g, c or t <400> 397 ttgtgaactc ttctattatt attaagtgtt gtcaattgtc agcatccata ttctattccg' 60 atgatgaata gaagcattat atttcagcat caaaatgcag ttggggtcgt aatgagcatc 120 attagggacc tta atg gga gtc aga act gta tgt cat ttt att cag gtt 169 Met Gly Val Arg Thr Val Cys His Phe Ile Gln Val -25 -20 ttt cta agt tta ttt gtg ttt ttt tgg tta gtt ggt ttt tct ttt ttc 217 Phe Leu Ser Leu Phe Val Phe Phe Trp Leu Val Gly Phe Ser Phe Phe -10 - 5 ttt ttt tta cdb ttt tct acc aag cag gtg aga gtw gaa cag cat tgt 265 Phe Phe Leu Xaa Phe Ser Thr Lys Gln Val Arg Val Glu Gln His Cys 10 qat ttt aaa agt aca cca nnd gta gag tct tcc agt acc gtt ggc cat 313 Asp Phe Lys Ser Thr Pro Xaa Val Glu Ser Ser Ser Thr Val Gly His 25 316 gcc Ala 35 <210> 398 <211> 251 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 63..251 <221> sig_peptide <222> 63..143 <223> Von Heijne matrix score 5 seq LSCFYLLAIVSNA/VM <400> 398 atgttgtage ttetgteata attteettee ettttaagge tgaataattt teeattgtgt 60 107 at atq tac cat att ttg ttc atc cat tca ttc att gat aga tac ttg Met Tyr His Ile Leu Phe Ile His Ser Phe Ile Asp Arg Tyr Leu -20 agt tgc ttc tac ctt ttg gca att gtg agt aat gct gtt atg aac atg 155 Ser Cys Phe Tyr Leu Leu Ala Ile Val Ser Asn Ala Val Met Asn Met -5 ggt gta caa atg tot gtt ttg agt oot tgt ttt gct ttc gtg cat tot 203 Gly Val Gln Met Ser Val Leu Ser Pro Cys Phe Ala Phe Val His Ser 10 15 att aaa aat gtt aag gtt ctt tgc ttt tta ctt ttt ttt ctc ttt ggg 251 Ile Lys Asn Val Lys Val Leu Cys Phe Leu Leu Phe Phe Leu Phe Gly 25 <210> 399 <211> 120 <212> DNA <213> Homo sapiens <220> <221> CDS

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                                                                        51
          Met Gln Phe Thr Val Leu Met Cys Pro Val Gln Trp Leu Leu
                  -20
                                       -15
                                                                        99
gtg tat tca ccc agt tgt gca gcc acc atc aca gtc aat ttt aaa aca
Val Tyr Ser Pro Ser Cys Ala Ala Thr Ile Thr Val Asn Phe Lys Thr
            -5
ttt tca tca ccc caa acc ggg
                                                                       120
Phe Ser Ser Pro Gln Thr Gly
<210> 400
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<212> DNA
<213> Homo sapiens
<220>
<221> CDS
<222> 342..461
<221> sig_peptide
<222> 342..452
<223> Von Heijne matrix
      score 5
      seq VSCLSAGLRVCCS/QR
<221> misc feature
<222> 246,260
<223> n=a, g, c or t
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etetgteece geggetgggt etegtetget eeggtteetg ggeteetaat tettggteea
                                                                       120
gettetteca ggeacatect ettetetgee etcegtecat titiggageeg gagatggtgg
                                                                       180
gctkggggcc gccccagtag tgagacagtg gaagtaaacc ccatctgccg ttcccgtgcg
                                                                       240
taqaqaaaaa cgttgaccgc gaggctgggg aggagagttg cctctgagga agaagggcac
                                                                       300
aqaqanccaa aattagtttn gaaagcatcc tgatttggtg cccgaggcct ggaaagaaat
ggcggctggg gtgcggcgga ggtaggggag gaaaacgttg g atg aga agg gcc tgg
                                                                       356
                                               Met Arg Arg Ala Trp
                                                        ~35
                                                                       404
act cag gaa agg gaa ccg cgt ccg tgt gag ccc gct gag cgc gca gac
Thr Gln Glu Arg Glu Pro Arg Pro Cys Glu Pro Ala Glu Arg Ala Asp
                                                 -20
        -30
                             -25
cet gee cet gte tee tgt etg tet gea ggt etg ege gte tgt tgt tee
                                                                       452
Pro Ala Pro Val Ser Cys Leu Ser Ala Gly Leu Arg Val Cys Cys Ser
    -15
                        -10
                                                                       463
cag cgc tct gc
Gln Arg Ser
<210> 401
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<221> sig peptide

<222> 94..168

seq DFFICLLAICVSS/FE

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tggttttgat ttgcatttcc ctgatcatta gtg atg ttg cat ttg att tgc att

Met Leu His Leu Ile Cys Ile

-25 -20

tcc ctg atc gtt aat gat ttt ttc ata tgt ttg ttg gcc att tgc gta 162 Ser Leu Ile Val Asn Asp Phe Phe Ile Cys Leu Leu Ala Ile Cys Val

-15 -10 -5

tct tct ttt gag aat tgt cta ttt atg tcc tta gcc cac agt gg 206 Ser Ser Phe Glu Asn Cys Leu Phe Met Ser Leu Ala His Ser 1 5

<210> 402

<211> 330

<212> DNA

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<221> CDS

<222> 42..329

<221> sig_peptide

<222> 42..230

<223> Von Heijne matrix
score 4.90000009536743
seq VTSLANLIPPVKA/XP

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-60

152

296

ccc atg gtg tgg tgc tgc ctc ttt gtc cgt tcg cag cga aaa cgg aaa 104
Pro Met Val Trp Cys Cys Leu Phe Val Arg Ser Gln Arg Lys Arg Lys
-55
-50
-45

cag agc acc caa gat gaa gat gct gtt agc ctt tgc agt ctc gac ata Gln Ser Thr Gln Asp Glu Asp Ala Val Ser Leu Cys Ser Leu Asp Ile

-40 -35 -30

agt gag cct agt aat aaa cgg gtc aaa ccc ctt tcc cga gtc acg tcg
Ser Glu Pro Ser Asn Lys Arg Val Lys Pro Leu Ser Arg Val Thr Ser

-25 -20 -15

cta gca aac ctc atc ccg ccc gtg aag gcc ayg cca tta aag cgc ttc 248

Leu Ala Asn Leu Ile Pro Pro Val Lys Ala Xaa Pro Leu Lys Arg Phe

-10 -5 1 5

agt caa acc ctg cag cgc tcc att agc ttc cgc agt gag agt cgc cct Ser Gln Thr Leu Gln Arg Ser Ile Ser Phe Arg Ser Glu Ser Arg Pro

10 15 20

gac atc ctc gcc ccc cga ccc tgg tcc aga aat g 330
Asp Ile Leu Ala Pro Arg Pro Trp Ser Arg Asn

<210> 403

<211> 311

<212> DNA

<213> Homo sapiens

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 gcttatctgt tggtaatttt tatttagatc aagttaaaca taaatgactt tgcattactc
                                                                        120
 tttggtcact ttttcctagt catttcaaat agtctgtctt atttctc atg gtt ttt
                                                                        176
                                                       Met Val Phe
                                                       -20
 tgg aca aaa ttt tgt att tta att agt aca gca ttt cct tct tta ttg
                                                                        224
 Trp Thr Lys Phe Cys Ile Leu Ile Ser Thr Ala Phe Pro Ser Leu Leu
          -15
                              -10
 aca cag att att ttc cct aaa tct att aca ttt gct ttc cag ttt ttc
                                                                        272
 Thr Gln Ile Ile Phe Pro Lys Ser Ile Thr Phe Ala Phe Gln Phe Phe
                      5
                                          10
                                                                        311
 tgg aac agg gaa aaa caa aaa aca aaa aca cca act ggg
 Trp Asn Arg Glu Lys Gln Lys Thr Lys Thr Pro Thr Gly
                  20
 <210> 404
  <211> 274
  <212> DNA
  <213> Homo sapiens
  <220>
  <221> CDS
  <222> 80..274
  <221> sig_peptide
  <222> 80..190
  <223> Von Heijne matrix
        score 4.90000009536743
        seq MLIMLGIFFNVHS/AV
  <400> 404
  ccctgcgagg gcatcctggg ctttctccca ccgctttccg agcccgcttg cacctcggcg
                                                                         60
                                                                        112
  atcoccquet coettett atg geg teg etc etg tge tgt ggg eeg aag etg
                       Met Ala Ser Leu Leu Cys Cys Gly Pro Lys Leu
                               -35
                                                    -30
                                                                         160
  gcc gcc tgc ggc atc gtc ctc agc gcc tgg gga gtg atc atg ttg ata
  Ala Ala Cys Gly Ile Val Leu Ser Ala Trp Gly Val. Ile Met Leu Ile
                          -20
  atg ctc gga ata ttt ttc aat gtc cat tcc gct gtg ttg att gag gac
                                                                         208
  Met Leu Gly Ile Phe Phe Asn Val His Ser Ala Val Leu Ile Glu Asp
  gtt ccc ttc acg gag aaa gat ttt gag aat ggc ccc cag aac ata tac
                                                                         256
  Val Pro Phe Thr Glu Lys Asp Phe Glu Asn Gly Pro Gln Asn Ile Tyr
              10
                                  15
                                                                         274
  aac ctt tac gag cat ggg
  Asn Leu Tyr Glu His Gly
  <210> 405
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                                                                         60
gcccaaga atg tct gtc tca gct ctg ctt cta gag mtc ctc caa gmt gcc
                                                                        110
          Met Ser Val Ser Ala Leu Leu Leu Glu Xaa Leu Gln Xaa Ala
              -15
                                   -10
 atc cct cgy mam acc tca ggc ttm caa gac ctg ccc aac tgg g
                                                                        153
 Ile Pro Arg Xaa Thr Ser Gly Xaa Gln Asp Leu Pro Asn Trp
                         5
 <210> 406
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 <212> DNA
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       seq VIAIVSFTTLCSS/LY
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· aaataaaaaa tattaaaaaa taatctcatc tttgatttta gatttagggg gtgtgc atg
                                                                         59
                                                                        107
 caq gct tgt tat atg ggt atg tgg tat act gcc gag gct tgg ggt acg
 Gln Ala Cys Tyr Met Gly Met Trp Tyr Thr Ala Glu Ala Trp Gly Thr
                                  -30
 att gag tcc ctc acc cag gta gtg agc gta atc gca ata gtt agt ttt
                                                                        155
 Ile Glu Ser Leu Thr Gln Val Val Ser Val Ile Ala Ile Val Ser Phe
         -20
 aca acc ctg tgc tcc tct ctg tat tcc ccc caa gta gtc ccc agt gtt
                                                                        203
 Thr Thr Leu Cys Ser Ser Leu Tyr Ser Pro Gln Val Val Pro Ser Val
                                                                        206
 999
 Gly
 <210> 407
 <211> 479
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seq PLAACPLLLPIFS/HA

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<210> 409 <211> 341

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gtgttgcaga aatccggcaa tcgacctgag gacttgcgag ccgctcagct cccgggacgt
                                                                       60
ttggagctgc tgctaaataa tttctgctca gcc atg tcg ccg gct cca gat gca
                                                                       114
                                     Met Ser Pro Ala Pro Asp Ala
ged deg get det gegiteg ate ted etg ttt gad etd age geg gat get
                                                                      162
Ala Pro Ala Pro Ala Ser Ile Ser Leu Phe Asp Leu Ser Ala Asp Ala
                -30
                                     -25
ccg gtc ttt cag ggc ctg agc ctg gtg agc cac gcg cct ggg gag gct
                                                                      210
Pro Val Phe Gln Gly Leu Ser Leu Val Ser His Ala Pro Gly Glu Ala
            -15
                                 -10
ctg gcc cgg gct ccg cgt act tcc tgt tca ggc tca ggg gag aga gaa
                                                                      258
Leu Ala Arg Ala Pro Arg Thr Ser Cys Ser Gly Ser Gly Glu Arg Glu
ago coa gaa aga aag ota oto cag ggt oot atg gat att toa gag aag
                                                                      306
Ser Pro Glu Arg Lys Leu Leu Gln Gly Pro Met Asp Ile Ser Glu Lys
                    20
                                         25
tta ttt tgt tca act tgt gac cag acc ttc cag aa
                                                                      341
Leu Phe Cys Ser Thr Cys Asp Gln Thr Phe Gln
                35
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<222> 153..320
<221> sig_peptide
<222> 153..257
<223> Von Heijne matrix
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      seq LFIFIGSLQPVPT/RF
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cacacacaaa ctctcaagtg gcctaattcc ctctcaccaa accaatcaca atacagataa
                                                                       60
aagagaataa cttgtgttca tttttgtaca aacaaaaaag atataaattg tgaatgrtgc
                                                                      120
atgrttttta awtwmccaag taaactgggc aa atg ctt ctg cat tat tta aag
                                                                      173
                                    Met Leu Leu His Tyr Leu Lys
                                     -35
cta aaa ggt gat cag tgg aaa ctt tcc tct gtt agt act cta ata ctt
                                                                      221
Leu Lys Gly Asp Gln Trp Lys Leu Ser Ser Val Ser Thr Leu Ile Leu
            -25
                                -20
ttt ata ttt atc ggc tca cta caa cct gtg cct acc agg ttc aag cga
                                                                      269
Phe Ile Phe Ile Gly Ser Leu Gln Pro Val Pro Thr Arg Phe Lys Arg
                            -5
tto too tgt oto gdo cac otg agt ago oga gao cac agg caa goa ota
                                                                      317
Phe Ser Cys Leu Xaa His Leu Ser Ser Arg Asp His Arg Gln Ala Leu
```

-40 tgg aaa cgc ctc ttc aca cta aag gaa gaa aaa cct aag atg tac ttc

-25

Trp Lys Arg Leu Phe Thr Leu Lys Glu Glu Lys Pro Lys Met Tyr Phe

atg acc atg atc gtt tcc ctt gct gcg gtt gct tgg gtg gga caa caa Met Thr Met Ile Val Ser Leu Ala Ala Val Ala Trp Val Gly Gln Gln

gtc cac aac ctg ctt ctc acc tac ctg ata gtg act tcc tta cta ttg

Val His Asn Leu Leu Leu Thr Tyr Leu Ile Val Thr Ser Leu Leu Leu

ctt cct gga cta aac caa cat gga atc att ttg aag tac att

Leu Pro Gly Leu Asn Gln His Gly Ile Ile Leu Lys Tyr Ile 25

497

545

593

635

<210> 412 <211> 335 <212> DNA <213> Homo sapiens

20

-30

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      seq LLRGLLAGPAATS/WS
<400> 412
aatggacgag aggtcagggt aggtttttga ag atg gcg gcc ctc aag gct ctg
                                                                        53
                                     Met Ala Ala Leu Lys Ala Leu
                                         -25
gtg tcc ggc tgt ggg cgg ctt ctc cgt ggg cta cta gcg ggc ccg gca
                                                                      101
Val Ser Gly Cys Gly Arg Leu Leu Arg Gly Leu Leu Ala Gly Pro Ala
                -15
                                     -10
gcg acc agc tgg tct cgg ctt cca gct cgc ggg ttc agg gaa gtg gtg
                                                                      149
Ala Thr Ser Trp Ser Arg Leu Pro Ala Arg Gly Phe Arg Glu Val Val
gag acc caa gaa ggg aag aca act ata att gaa ggc cgt atc aca gcg
                                                                      197
Glu Thr Glu Glu Gly Lys Thr Thr Ile Ile Glu Gly Arg Ile Thr Ala
                        20
act ccc aag gag agt cca aat cct cct aac ccc tct ggc cag tgc ccc
                                                                      245
Thr Pro Lys Glu Ser Pro Asn Pro Pro Asn Pro Ser Gly Gln Cys Pro
                    35
                                         40
atc tgc cgt tgg aac ctg aag cac aag tat aac tat gac gat gtt ctg
                                                                      293
Ile Cys Arg Trp Asn Leu Lys His Lys Tyr Asn Tyr Asp Asp Val Leu
                50
                                     55
ctg ctt agc cag ttc atc cgg cct cat gga ggc atg ctg ccc
                                                                      335
Leu Leu Ser Gln Phe Ile Arg Pro His Gly Gly Met Leu Pro
                                70
<210> 413
<211> 158
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<222> 25..156
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<222> 25..93
<223> Von Heijne matrix
     score 4.90000009536743
     seq LVGFKQVVAWTFA/SD
<221> misc feature
<222> 17
<223> n=a, g, c or t
<400> 413
agaaactgac atttgbntgt ttta atg ggg tcc ctg ctg ttc atc agg cag
                                                                       51
                           Met Gly Ser Leu Leu Phe Ile Arg Gln
                                        -20
aca ctt gtg ggc ttt aaa cag gtc gtt gct tgg acc ttt gct tct gat
                                                                       99
Thr Leu Val Gly Phe Lys Gln Val Val Ala Trp Thr Phe Ala Ser Asp
                -10
tca cat tgt gsa aaw gtg gww atg gtd wtc tws agt cag ttg arw aat
                                                                      147
Ser His Cys Xaa Xaa Val Xaa Met Val Xaa Xaa Ser Gln Leu Xaa Asn
                            10
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ccc cca ctg gg 158 Pro Pro Leu 20 <210> 414 <211> 202 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 59..202 <221> sig_peptide <222> 59..130 <223> Von Heijne matrix score 4.90000009536743 seq LLLRGSLLASXRA/XX <221> misc_feature <222> 160 <223> n=a, g, c or t <400> 414 etgggagega cegeteeget egtetegttg gtteeggagg tegetgegge ggtgggaa 58 atg ctg gcg cgc gcg gcg gag grc act ggg gcc ctt ttg ctg agg ggc 106 Met Leu Ala Arg Ala Ala Glu Xaa Thr Gly Ala Leu Leu Leu Arg Gly -20 -15 tet eta etg get tet gre ege gek yeg sys veg eet eet etg gga ttg 154 Ser Leu Leu Ala Ser Xaa Arg Ala Xaa Xaa Pro Pro Leu Gly Leu -5 see egn aac acc gwt ggt act gtt egt gee gea gea gge etg ggt 202 Xaa Arg Asn Thr Xaa Gly Thr Val Arg Ala Ala Gly Gly Leu Gly 10 15 <210> 415 <211> 229 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 146..229 <221> sig peptide <222> 146..196 <223> Von Heijne matrix score 4.90000009536743 seq LLSFCLCSDFISQ/DA <400> 415 gtmaaactcc cgcagacttc tctgtagatc gctgagcgat actttcggca gcacctcctt 60 gatteteagt tttgetggag geegeaacea ggeeetaete aaceeteett eecaggagge 120 ccaggccccc aagctcagat caccc atg aat gcc tcc ctc ttg tct ttc tgc 172 Met Asn Ala Ser Leu Leu Ser Phe Cys -15 ctt tgt tca gat ttc atc tct caa gat gcc ctc ctt ctc act gtc ata 220 Leu Cys Ser Asp Phe Ile Ser Gln Asp Ala Leu Leu Thr Val Ile 229 ttt cct ccc Phe Pro Pro 10

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<211> 265
<212> DNA
<213> Homo sapiens
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<221> CDS
<222> 27..263
<221> sig_peptide
<222> 27..206
<223> Von Heijne matrix
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      seq LVGVIVHSGQAHA/GH
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atgatgaaca aataaggttt ccctgg atg cta aac atg gag cct tac aca gtt
                             Met Leu Asn Met Glu Pro Tyr Thr Val
                             -60
                                                  -55
tca gga atg gct cgc caa gat tct tct tct gaa gtt ggg gaa aat ggg ,
                                                                       101
Ser Gly Met Ala Arg Gln Asp Ser Ser Ser Glu Val Gly Glu Asn Gly
    -50
                        -45
                                             -40
cga agt gtg gat cag ggc ggt gga gga tcc cca cga aaa aag gtt gcc
                                                                       149
Arg Ser Val Asp Gln Gly Gly Gly Ser Pro Arg Lys Lys Val Ala
-35
                    -30
                                         -25
ctc aca gaa aac tat gaa ctt gtc ggt gtc atc gta cac agt ggg cag
                                                                       197
Leu Thr Glu Asn Tyr Glu Leu Val Gly Val Ile Val His Ser Gly Gln
                -15
                                     -10
gca cac gca ggc cac tac tat tcc ttc att aag gac agg cga ggg tgt
                                                                       245
Ala His Ala Gly His Tyr Tyr Ser Phe Ile Lys Asp Arg Arg Gly Cys
gga aaa gga aag tgg ctg gg
                                                                       265
Gly Lys Gly Lys Trp Leu
   15
<210> 417
<211> 228
<212> DNA
<213> Homo sapiens
<220>
<221> CDS
<222> 160..228
<221> sig_peptide
<222> 160..219
<223> Von Heijne matrix
      score 4.90000009536743
      seq LHLXSSRXPPILA/SP
<221> misc_feature
<222> 166..167,190
<223> n=a, g, c or t
<400> 417
ttgtctgtct taggcctgga cactgttgtt gacttatttc cagattttaa tttctctttg
                                                                       60
gttgaagact gccaactgtc tcatagagtg tttgatttat ttatttatty athtwgacat
                                                                      120
gaggwykctc tctgcmaacc caggctggak tgcagtgac atg atv nng gct cac
                                                                      174
                                           Met Xaa Xaa Ala His
ttc agc ctc cac ctc nkg agc tca agg art cck ccc atc tta gcc tcc
                                                                      222
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227											
Phe Ser Leu His Leu Xaa Ser Ser Arg Xaa Pro Pro Ile Leu Ala Ser -15 -10 -5 1 cca gta	228										
Pro Val											
<210> 418 <211> 225 <212> DNA <213> Homo sapiens											
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<400> 418											
3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3	60 120 169										
	217										
cct gcg gg Pro Ala 15	225										
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<221> sig_peptide <222> 42128 <223> Von Heijne matrix score 4.80000019073486 seq LLSARLLSQEKRA/AE											
<400> 419 gtgctctatg gagctattgc ggccgtgggt ggtcgcgggc r atg cgg ggc tgc cag Met Arg Gly Cys Gln -25	56										
	104										
Leu Leu Gly Leu Arg Ser Ser Trp Pro Gly Asp Leu Leu Ser Ala Arg -20 -15 -10											
ctc ttg tcc caa gag aag cgg gca gcg gaa acg cac ttt ggg ttt gag Leu Leu Ser Gln Glu Lys Arg Ala Ala Glu Thr His Phe Gly Phe Glu -5 1 5	152										
act gtg tcg gaa gag gag aag agg ggg gac tta aca tca gtt gta agt Thr Val Ser Glu Glu Glu Lys Arg Gly Asp Leu Thr Ser Val Val Ser 10 20	200										
cta gag tac cct gaa gtg caa tta cag ggt caa agg gtc tat gcm ttc Leu Glu Tyr Pro Glu Val Gln Leu Gln Gly Gln Arg Val Tyr Ala Phe	248										

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25
                                         35
ctg tca ccc att tgt acc tat ggc tct gag gga tgc agc ctc aag
                                                                      293
Leu Ser Pro Ile Cys Thr Tyr Gly Ser Glu Gly Cys Ser Leu Lys
<210> 420
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<222> 30..194
<221> sig_peptide
<222> 30..134
<223> Von Heijne matrix
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      seg PWVLDIFLTLVFA/LG
<400> 420
agttgctaga aagcaatgcg cctattcac atg gag aat ctt ccc ttt cct cta
                                                                       53
                                Met Glu Asn Leu Pro Phe Pro Leu
                                -35
                                                    -30
aaa tta ctt agt gcc tca tca cta aac acc ccc agc tcc aca cca tgg
                                                                      101
Lys Leu Leu Ser Ala Ser Ser Leu Asn Thr Pro Ser Ser Thr Pro Trp
                            -20
gtg ttg gat atc ttc ctc acc ttg gtg ttt gcc ctg ggg ttc ttc ttc
                                                                      149
Val Leu Asp Ile Phe Leu Thr Leu Val Phe Ala Leu Gly Phe Phe
                        -5
cta tta ctc ccc tac ttc tct tac ctc cgt tgt gac aac cca cca
                                                                      194
Leu Leu Pro Tyr Phe Ser Tyr Leu Arg Cys Asp Asn Pro Pro
                10
<210> 421
<211> 90
<212> DNA
<213> Homo sapiens
<220>
<221> CDS
<222> 29..88
<221> sig_peptide
<222> 29..67
<223> Von Heijne matrix
      score 4.80000019073486
      seq MCVCVFAIFGVRC/CV
<221> misc feature
<222> 61
<223> n=a, g, c or t
<400> 421
tatttgggat ttgttgctct gtgtgtat atg tgc gtg tgt gtg ttt gct ata
                                                                       52
                               Met Cys Val Cys Val Phe Ala Ile
                                           -10
ttt ggg gtn cgt tgc tgt gtg tgt gtc cgc tgt att tg
                                                                       90
Phe Gly Val Arg Cys Cys Val Cys Val Arg Cys Ile
-5
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<210> 422

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<212> DNA
<213> Homo sapiens
<220>
<221> CDS
<222> 22..159
<221> sig_peptide
<222> 22..153
<223> Von Heijne matrix
      score 4.80000019073486
      seq XPCPLLFPGACFP/CP
<400> 422
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                                                                       51
                        Met Ile Cys Ile Phe Tyr Ser Lys Ile Ser
atc tct gtc ggc tgt ggg agg aca gcc gag caa gtt gga tgt aaa
                                                                        99
Ile Ser Val Gly Cys Gly Arg Thr Ala Ala Glu Gln Val Gly Cys Lys
                -30
                                    -25
cag agg tca ttt cac ckc ccy tgc cct ctg ctg ttt cct ggt gcd tgc
                                                                      147
Gln Arg Ser Phe His Xaa Pro Cys Pro Leu Leu Phe Pro Gly Ala Cys
            -15
ttt ccc tgc cca ac
                                                                      161
Phe Pro Cys Pro
<210> 423
<211> 420
<212> DNA
<213> Homo sapiens
<220>
<221> CDS
<222> 333..419
<221> sig_peptide
<222> 333..380
<223> Von Heijne matrix
      score 4.80000019073486
      seq ICVSLMASDGASS/PV
<221> misc feature
<222> 323..324,328
<223> n=a, g, c or t
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ctgccgcygg acacgggttc ttccagcttt tggctattgt gaataacgct gctatggaca
                                                                       60
tgaatgtaca aacatccctt cagatcctcc tttcagttct tgtgggtaca taccccgagt
                                                                       120
ggaactgtgg catcatatgg taactctgtg tttaacattt tgaggaacca ccctactgct
                                                                       180
                                                                       240
teccaeagag getgtaceag tttaettece accaacagtg caaggattee aattteteca
                                                                       300
catccgtgcc aacactattt tctttttgtc gctgttgtca ttgtttgtct ggaaaatagc
catgctgagg ggtgagaggt grnnghanrg tt atg aat ttg att tgc gtt tcc
                                                                       353
                                     Met Asn Leu Ile Cys Val Ser
ctg atg gcc agt gat ggg gca tct tcc cct gtg ctt ggt ggc tct tca
                                                                       401
Leu Met Ala Ser Asp Gly Ala Ser Ser Pro Val Leu Gly Gly Ser Ser
                -5
                                     1
cac tct tcc tcc cwt rgg g
                                                                       420
His Ser Ser Ser Xaa Xaa
        10
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<210> 424
<211> 432
<212> DNA
<213> Homo sapiens
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<221> CDS
<222> 256..432
<221> sig_peptide
<222> 256..396
<223> Von Heijne matrix
     score 4.80000019073486
     seg LVSALPQASFSSS/SE
<400> 424
60
120
ggaggaaggg agggggagag acagagacct agaggggctg aagacccaga cagagctggc
                                                                 180
agagctactg agaagaggac tggagcgctc tgagagcctc tcaagatctt ttgggggagc'
                                                                 240
ccaataaatg tgaac atg gga tot gtc acr gga gct gtc ctc aag acg cta
                                                                 291
                Met Gly Ser Val Thr Gly Ala Val Leu Lys Thr Leu
                        -45
                                           -40
ctt ctg tta tct act caa aat tgg aac aga gtc gaa gct ggg aat tcc
                                                                 339
Leu Leu Ser Thr Gln Asn Trp Asn Arg Val Glu Ala Gly Asn Ser
                   -30
                                      -25
tat gac tgt gat gat cet ett gtg tet gee ttg eet eag gea tee tte
                                                                 387
Tyr Asp Cys Asp Asp Pro Leu Val Ser Ala Leu Pro Gln Ala Ser Phe
               -15
                                  -10
age agt tot too gag oto too age agt cat agt cot gga ttt gca
                                                                 432
Ser Ser Ser Ser Glu Leu Ser Ser Ser His Ser Pro Gly Phe Ala
<210> 425
<211> 419
<212> DNA
<213> Homo sapiens
<220>
<221> CDS
<222> 278..418
<221> sig_peptide
<222> 278..370
<223> Von Heijne matrix
     score 4.80000019073486
     seq FFLLFLFSSCDVP/VP
<400> 425
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                                                                  60
tgcagcacqt tcttaggaat ggaatagaga agcatcctaa gccagaagga ttttttttt
                                                                 120
tctagatcac agtgaagctt taatatggkk ggatatttgt cccagcccaa atcccatgct
                                                                 180
gaattgaaac ccctagtgct ggaggtgggg cctggtggaa ggtgtttgga tcatgaggac
                                                                 240
acatetetga tgaatggeet ageteateet ettagtg atg atg agt gag tye tea
                                                                 295
                                      Met Met Ser Glu Xaa Ser
                                          -30
caa gat ctg gtt gta aag tgt gcc cca cca csg cca ttc ttt ctc ttg
                                                                 343
Gln Asp Leu Val Val Lys Cys Ala Pro Pro Xaa Pro Phe Phe Leu Leu
                   -20
                                      -15
ttc ctg ttt tct tca tgt gat gtg cct gtt ccc ctt cac ctt ctg caa
                                                                 391
Phe Leu Phe Ser Ser Cys Asp Val Pro Val Pro Leu His Leu Leu Gln
               -5
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				ttc Phe					g								419
<211 <212	0> 42 L> 23 2> Di B> Ho	32 1A	sapi	ens													
)> L> CI 2> 54		30 [°]														
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seq VLLTSGVKPQTFA/VS <400> 426 gcagtgagtg ttacagttct taaagatggt gtgtccggag tttgttcctt cca atg Met ttc aga tgt gtc cgg ttt ctt cct tct ggc ggg ttc gtg gtc ttg ctg																56	
ttc Phe	aga Arg -25	tgt Cys	gtc Val	cgg Arg	ttt Phe	ctt Leu -20	cct Pro	tct Ser	ggc Gly	G] A aaa	ttc Phe -15	gtg Val	gtc Val	ttg	ctg	1	104
act Thr -10	tca	gga Gly	gtg Val	aag Lys	cca Pro -5	caa	acc Thr	ttc Phe	gca Ala	gtg Val 1	agt	gtt Val	aca Thr	gct Ala 5	ctt Leu	1	152
aaa	ggt Gly	ggc Gly	atg Met 10	ccc Pro	gga Gly	gtt Val	gtt Val	cat His	tcc Ser	tcc	ggt Gly	ggg Gly	ttc Phe 20	gtg	gtt Val	2	00
				gga Gly				aga		tc						2	232
<211 <212)> 42 L> 38 2> Di 3> Ho	3 NA	sapie	ens													
)> l> CI 2> 22		381														
<222	2> 22 3> Vo	on He	ijne 4.80	de mat 00000 ARLAG	1907		į										
)> 42 Jacat		acteo	aato	a ac	cacc	aacc	: tcc	iagec	·caa	atac	gctga	aa a	actat	tacc	-+	60
tcaa cago	acct gtct	cg g	gaato gtcao	ccac	g tt gt tg	ttcc	cctt	gac gtg	ttcc	tgt gac	caco	gtta cagg g at	iga g iga g ig ag it Ai	gaaaa gagc <u>g</u> ga gt	gtgg	ga 1 cc 1 gt 2	120 180 237
Arg	Arg -25	Glu	Gly	His	Pro	Leu -20	Phe	Pro	Asn	Val	Pro -15	cgc Arg	Cys	Leu	Phe	· 2	285
tta Leu -10	aac Asn	gct Ala	cgg Arg	ttg Leu	gcg Ala	gga Gly	acc Thr	ctg Leu	tgc Cys	cag Gln 1	ctg Leu	aaa Lys	ctc Leu	ctt Leu 5	cag Gln	3	333

ttt ggc cgc cta gga aac acc gag agt cac cta cat ggg ctg gct ggg 381 Phe Gly Arg Leu Gly Asn Thr Glu Ser His Leu His Gly Leu Ala Gly 10 15 99 383 <210> 428 <211> 132 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 32..130 <221> sig_peptide <222> 32..124 <223> Von Heijne matrix score 4.80000019073486 seq LLCPLTCPHHSLS/TV <400> 428 ttcaacaaat gagtcatagt gttttcgtat t atg tat ttt gat atc cag att 52 Met Tyr Phe Asp Ile Gln Ile -30 gtc tca gat gtg gtc agc ggg att ccc ttc aaa ctt ctg tgc cct tta 100 Val Ser Asp Val Val Ser Gly Ile Pro Phe Lys Leu Leu Cys Pro Leu -20 aca tgt ccc cat cat tct ctg agc acc gtg gg 132 Thr Cys Pro His His Ser Leu Ser Thr Val <210> 429 <211> 165 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 25..165 <221> sig_peptide <222> 25..117 <223> Von Heijne matrix score 4.80000019073486 seq FSPFLPSLPLLEA/ER caaactgttg aaaagttaac tett atg tta ttt ata ttt tea gae ata gat 51 Met Leu Phe Ile Phe Ser Asp Ile Asp -30 -25 tgg aag atg gac tta tgc ttt ttc tct ttc tct cct ttc ctt ccc tcc 99 Trp Lys Met Asp Leu Cys Phe Phe Ser Phe Ser Pro Phe Leu Pro Ser -15 ctt cct ttg ttg gag gct gaa aga atg agg gtc agt gat caa ctt cag 147 Leu Pro Leu Leu Glu Ala Glu Arg Met Arg Val Ser Asp Gln Leu Gln tat acc act gga kac ggg 165 Tyr Thr Thr Gly Xaa Gly <210> 430

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<212> DNA

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                                                                         60
 accettgate geacteaga accaeagtta aaacctcttt geagcttcte aggactcaec
                                                                        120
 tggaaccaac gggcacagtt ggcaacacca tc atg aca tca caa cct gtt ccc
                                                                        173
                                      Met Thr Ser Gln Pro Val Pro
                                                       -65
 aat gag acc atc ata gtg ctc cca tca aat gtc atc aac ttc tcc caa
                                                                        221
 Asn Glu Thr Ile Ile Val Leu Pro Ser Asn Val Ile Asn Phe Ser Gln
                              -55
                                                  -50
 gca gag aaa ccc gaa ccc acc aac cag ggg cag gat agc ctg aag aaa
                                                                        269
 Ala Glu Lys Pro Glu Pro Thr Asn Gln Gly Gln Asp Ser Leu Lys Lys
                          -40
                                              -35
 cat cta cac gca gaa atc aaa gtt att ggg act atc cag atc ttg tgt
                                                                        317
 His Leu His Ala Glu Ile Lys Val Ile Gly Thr Ile Gln Ile Leu Cys
                      -25
                                          -20
 ggc atg atg gta ttg agc ttg ggg atc att ttg gca tct gct tcc ttc
                                                                        365
 Gly Met Met Val Leu Ser Leu Gly Ile Ile Leu Ala Ser Ala Ser Phe
                  -10
                                      -5
 tct cca aat ttt acc caa gtg act tct aca ctg ttg aac tct gct tac
                                                                        413
 Ser Pro Asn Phe Thr Gln Val Thr Ser Thr Leu Leu Asn Ser Ala Tyr
                             10
                                                  15
 cca ttc ata gga ccc ggg
                                                                        431
 Pro Phe Ile Gly Pro Gly
     20
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                                          Met Val Asp Glu Cys Leu
                                          -40
 aca gag cct gtg tgg gga agc aaa agg caa ggg tgt agt tca cag gca
                                                                       102
. Thr Glu Pro Val Trp Gly Ser Lys Arg Gln Gly Cys Ser Ser Gln Ala
                 -30
                                      -25
                                                          -20
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235	
gaa gcg agc tgt gac att gtc agt gca gcg tgt aag tgt ggc tcc tca Glu Ala Ser Cys Asp Ile Val Ser Ala Ala Cys Lys Cys Gly Ser Ser -15 -10 -5	150
cag gcg gcc att gat tgt gag acc tca tct tgc tct gaa gat ttc ccg Gln Ala Ala Ile Asp Cys Glu Thr Ser Ser Cys Ser Glu Asp Phe Pro 1 5 10	198
gtg Val 15	201
<210> 434 <211> 334 <212> DNA <213> Homo sapiens	
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gga tac ggc tct ctg atg gct cct tct agc cct acc cct tct ggg Gly Tyr Gly Ser Leu Met Ala Pro Ser Ser Pro Thr Pro Ser Gly 5 10 15	334
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ttc tac ctc acg gtc aag aga gcg aac tgc agc ctg gag cta cct ccg Phe Tyr Leu Thr Val Lys Arg Ala Asn Cys Ser Leu Glu Leu Pro Pro -50 -45 -40 -35	220
gcc agc ggt ccg gcc aag gac gct gag gag cct agt aat aaa cgg gtc Ala Ser Gly Pro Ala Lys Asp Ala Glu Glu Pro Ser Asn Lys Arg Val	268

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-25
                -30
                                                         -20
aaa ccc ctt tcc cga gtc acg tcg cta gca aac ctc atc ccg ccc gtg
                                                                      316
Lys Pro Leu Ser Arg Val Thr Ser Leu Ala Asn Leu Ile Pro Pro Val
                                -10
aaq qcc acg cca tta aag cgc ttc agt caa acc ctg cag cgc tcc att
                                                                       364
Lys Ala Thr Pro Leu Lys Arg Phe Ser Gln Thr Leu Gln Arg Ser Ile
                                                                       386
age tte ege agt gag age gee t
Ser Phe Arg Ser Glu Ser Ala
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gcgagcatcc tggccagaac aagccaagga gccaagacga gagggacaca cggacaaaca
acagacagaa gacgtactgg ccgctggact ccgctgcctc ccccatctcc ccgccatctg
                                                                       180
                                                                       229
egeceggagg atg age eea gee tte agg gee atg gat gtg gag eee ege
           Met Ser Pro Ala Phe Arg Ala Met Asp Val Glu Pro Arg
                       -25
                                            -20
gcc aaa ggc gtc ctt ctg gag ccc ttt gtc cac cag gtc ggg ggg cac
                                                                       277
Ala Lys Gly Val Leu Leu Glu Pro Phe Val His Gln Val Gly Gly His
-15
                    -10
                                         -5
                                                                       325
tea tgc gtg etc ege ttc aat gag aca ace etg tgc aag eec etg gtc
Ser Cys Val Leu Arg Phe Asn Glu Thr Thr Leu Cys Lys Pro Leu Val
                                10
cca agg gaa cat cag ttc tac gag acc ctc cct gct gag atg cgc aaa
                                                                       373
Pro Arg Glu His Gln Phe Tyr Glu Thr Leu Pro Ala Glu Met Arg Lys
                            25
                                                 30
                                                                       421
ttc act ccc cag tac aaa gga caa agc caa agg ccc ctt gtt agc tgg
Phe Thr Pro Gln Tyr Lys Gly Gln Ser Gln Arg Pro Leu Val Ser Trp
                        40
                                             45
                                                                       469
cca tcc ctq ccc cat ttt ttc ccc tgg tcc ttt ccc ctg tgg cca cag
Pro Ser Leu Pro His Phe Pro Trp Ser Phe Pro Leu Trp Pro Gln
                                                                       472
gga
Gly
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<221> misc feature

<213> Homo sapiens

score 4.80000019073486 seq ILAFLQSPRAILP/GN

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cttttgcctt gcaggattct ttttcatctt tgcagggact tctggggccg gagtatgtaa
                                                                      120
aactcctggg tctctgtgtg tgcctgagtg gctgctctac tgagactctg catacacagc
                                                                      180
tetgtatate ggacceawgg ceetggtgge atg ggc tea ega gga gat eee etg
                                                                      234
                                 Met Gly Ser Arg Gly Asp Pro Leu
atc tgt ggg ttg caa aga tct gtg gga gaa gtg tgg ttt cct gga tgg
                                                                      282
Ile Cys Gly Leu Gln Arg Ser Val Gly Glu Val Trp Phe Pro Gly Trp
                            -30
ggt cac aca atc act cac tgc ttc cct tgg ctg gag gtg ggg ctt ttt .
                                                                      330
Gly His Thr Ile Thr His Cys Phe Pro Trp Leu Glu Val Gly Leu Phe
                        -15
                                             -10
ttt tgg ctc cat gct cct ggg cgg gcg att gcc cta ccc cat ttt
                                                                      378
Phe Trp Leu His Ala Ala Pro Gly Arg Ala Ile Ala Leu Pro His Phe
tct tca ttc tct gtg ggt caa gdb gtt cac ttg gtc agt cca ttg tgr
                                                                      426
Ser Ser Phe Ser Val Gly Gln Xaa Val His Leu Val Ser Pro Leu Xaa
                                20
gam ctg gat att tca gtt gaa
                                                                      447
Xaa Leu Asp Ile Ser Val Glu
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<221> misc feature
<222> 20,279..281
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                                                                       60
ccatttatcg cttgagatct ccagccttac cgcggctcga aatggacccc aactgctcct
                                                                      120
geaceaetgg tgteteewre geetgeaeeg geteetgeae gtgeaaagag tgeaa atg
                                                                      178
cac ctc ctg caa gaa gag ctg ctg ctc ctg ctg ccc cgt ggg ctg tgc
                                                                      226
His Leu Leu Gln Glu Glu Leu Leu Leu Leu Pro Arg Gly Leu Cys
            -15
                                -10
caa gtg tgc cca cgg ctg tgt ctg caa agg gmc gtt gga gaa ctg cag
                                                                      274
Gln Val Cys Pro Arg Leu Cys Leu Gln Arg Xaa Val Gly Glu Leu Gln
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1
                                             10
mtg cnn nky cct gat gtg gga aca gct ctt ctc cca gat gtt aat aga
                                                                     322
Xaa Xaa Yaa Pro Asp Val Gly Thr Ala Leu Leu Pro Asp Val Asn Arg
                                         25
aca agc tgc aca acc tgg
                                                                       340
Thr Ser Cys Thr Thr Trp
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                                                                       120
gattggtgag ctgagtggag aagtgccata gagcggtgtt ttgccagagt gtctgcggat
                                                                      180
tgctcatacc tgggaaggat tctttgtatg gttcccttag gctgagggag ggtatcagct
                                                                       240
ttacagacct tgtgggatta caaaagggcc accacacact cttcaaccaa t atg tgt
                                                                       297
                                                          Met Cys
cta tct tgc att caa ggc tca ttc ttt gtt gaa att ttg cag ttg gtc
                                                                       345
Leu Ser Cys Ile Gln Gly Ser Phe Phe Val Glu Ile Leu Gln Leu Val
                         -20
act agg cta ttg tta tct cca tct caa agt aca cag aca cac aca cac
Thr Arg Leu Leu Ser Pro Ser Gln Ser Thr Gln Thr His Thr His
-10
aca cac aca cac aca a
                                                                       409
Thr His Thr His Thr
             10
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totgttottt tataggaaga aaaaacatag ttatttttot tttatgatac aaaggtatgo

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240	180												
tttctatgca agctggatac Cagaccaaga ataataaatc acaatttcat aaggtttcta agacttgata ttatatgggg at atg acc att ttg agg gaa atg tnn nca tca Met Thr Ile Leu Arg Glu Met Xaa Xaa Ser -30 -25													
ctt tat gta ctt gaa gct aag gat act gct atc tta ttg ctt gtt tna Leu Tyr Val Leu Glu Ala Lys Asp Thr Ala Ile Leu Leu Leu Val Xaa -20 -15 -10 '	280												
gtg agc gat aag aat gaa cag cag ctt ggg agg ggc gtg g Val Ser Asp Lys Asn Glu Gln Gln Leu Gly Arg Gly Val -5 1 5	320												
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tcc tgt ggg ttg cct gtt aag act ttg cca ttt atc tgt tgc aat ctt Ser Cys Gly Leu Pro Val Lys Thr Leu Pro Phe Ile Cys Cys Asn Leu -20 -15 -10	164												
tat ttc ttg ctg ttt tgt agg agt tct ttt tta tat ttt gga tat gat Tyr Phe Leu Phe Cys Arg Ser Ser Phe Leu Tyr Phe Gly Tyr Asp -5 1 5 .	212												
CCC att aat act tac atg tat tac aat gtt ttc tcc cac tcg gg Pro Ile Asn Thr Tyr Met Tyr Tyr Asn Val Phe Ser His Ser 10 15 20	256												
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gcg gas cgc ttc tct ccg ggc tct cgg ggc agg ggt tcg gac ttg gaa Ala Xaa Arg Phe Ser Pro Gly Ser Arg Gly Arg Gly Ser Asp Leu Glu -55 -50 -45	100												

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241

agg ggt ctg tgc ccc gcc cat ccc ggg gcc cct cct ttg ccc cgc ccc 148 Arg Gly Leu Cys Pro Ala His Pro Gly Ala Pro Pro Leu Pro Arg Pro -35 -30 ccg gac cgc ctt ccc cat tca ttc tct cct acg ggg tgt ctc ctg hgc 196 Pro Asp Arg Leu Pro His Ser Phe Ser Pro Thr Gly Cys Leu Leu Xaa -20 -15 ccc ctt ctg gtc tcg tgt ttg ggg tct ctg ctt ccg gtc acc caa acc 244 Pro Leu Leu Val Ser Cys Leu Gly Ser Leu Leu Pro Val Thr Gln Thr ctg ggg tcc ttc agt gct ggt ccc tgc ttc agg acc ctc a 284 Leu Gly Ser Phe Ser Ala Gly Pro Cys Phe Arg Thr Leu 10 15 . <210> 445 <211> 240 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 103..240 <221> sig_peptide <222> 103..177 <223> Von Heijne matrix score 4.69999980926514 seq ILXSLSSSVPSRA/GS <400> 445 tettttgtaa tgaageatgg cagecaggee tageacaett eeetetqeac accateetqe 60 teaggeetet gtgeetegge tgtgetgtte ettetgettg ga atg eat tea etq 114 Met His Ser Leu tgt cca ctt agc caa ttc cta cct att ctt tma agc ctc agt tcc agt 162 Cys Pro Leu Ser Gln Phe Leu Pro Ile Leu Xaa Ser Leu Ser Ser Ser -20 -15 -10 gtc ccc tcg agg gca ggc agt gct ttc cca tct gcc cta ggt cca ctc 210 Val Pro Ser Arg Ala Gly Ser Ala Phe Pro Ser Ala Leu Gly Pro Leu tac cag cct cta ctt ggg ccc cca gca tgg 240 Tyr Gln Pro Leu Leu Gly Pro Pro Ala Trp <210> 446 <211> 184 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 8..184 <221> sig_peptide <222> 8...139 <223> Von Heijne matrix score 4.69999980926514 seq LVFLSVXLLFLLF/LV 49 Met Arg Thr Gln Val Tyr Glu Gly Leu Cys Lys Asn Tyr Phe -40 tct ctt gct gta cta caa aga gat aga atc aaa ctg ctt ttt ttc gac

242 Ser Leu Ala Val Leu Gln Arg Asp Arg Ile Lys Leu Leu Phe Phe Asp -25 -20 ata ctg gtt ttt ctt tct gtt tww ctt ctc ttt ctt cta ttt ctt gtg 145 Ile Leu Val Phe Leu Ser Val Xaa Leu Leu Phe Leu Leu Phe Leu Val - 5 gat atw atg gct aat adc aca aca agt tta ggg agg ccc 184 Asp Ile Met Ala Asn Xaa Thr Thr Ser Leu Gly Arg Pro 10 <210> 447 <211> 360 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 34..360 <221> sig peptide <222> 34..168 <223> Von Heijne matrix score 4.69999980926514 seq LLSLAQTTTKTTA/TT <221> misc_feature <222> 280 <223> n=a, g, c or t aaaaactctt ttctttatcc tctttccaga aaa atg ggc caa ttc aca gct gca Met Gly Gln Phe Thr Ala Ala -45 atg gtt ggg aga att tcc tgt ctg gga gtc tgg aaa ctg cca aga gtg 102 Met Val Gly Arg Ile Ser Cys Leu Gly Val Trp Lys Leu Pro Arg Val -35 -30 gaa age tge age cag cca geg agg cct ctg ttg tca ctg gee caa aca 150 Glu Ser Cys Ser Gln Pro Ala Arg Pro Leu Leu Ser Leu Ala Gln Thr -15 198 Thr Thr Lys Thr Thr Ala Thr Thr Thr Thr Thr Lys His Ala Thr tgt gca ctg gca tat aca aac acg ccc aca gaa cca vrc caa gcg gac 246 Cys Ala Leu Ala Tyr Thr Asn Thr Pro Thr Glu Pro Xaa Gln Ala Asp 20 aag gct tca agg aga gct tct ggg ahv ctc rwv ncc gcg gcg agg cat 294 Lys Ala Ser Arg Arg Ala Ser Gly Xaa Leu Xaa Xaa Ala Ala Arg His 35 atc cct tgg cat ggt gcc act gca gcc cag ctc cca gcc ccc ccg cca 342 Ile Pro Trp His Gly Ala Thr Ala Ala Gln Leu Pro Ala Pro Pro Pro 45 tct gtc atc agc gct ctg 360 Ser Val Ile Ser Ala Leu 60 <210> 448 <211> 123 <212> DNA <213> Homo sapiens <220> <221> CDS

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                                          Met Leu Ile Phe Ile Ile
                                                       -15
gct att tta ttt ccc aat tca gga tca tgc ttt gca ttt agt tgt cat
                                                                      104
Ala Ile Leu Phe Pro Asn Ser Gly Ser Cys Phe Ala Phe Ser Cys His
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                            -5
gtc tcc ttt ttt ttt ttt t
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Val Ser Phe Phe Phe
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                   Met Val Arg Cys Ala Cys Phe Pro Phe Pro
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                                       -10
ttc gcc ttc tgc cat gac tgt aag ttt ctt ggg gcc tcc cag tca tgc
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Phe Ala Phe Cys His Asp Cys Lys Phe Leu Gly Ala Ser Gln Ser Cys
ttc ttg tta agc cgg caa aac tgt gta agc aca gga kga cct tca tcc
                                                                      146
Phe Leu Leu Ser Arg Gln Asn Cys Val Ser Thr Gly Xaa Pro Ser Ser
                            20
aaa tot gat ato aac toa agg tot gga tot tgt toa otg goa agg gg
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Lys Ser Asp Ile Asn Ser Arg Ser Gly Ser Cys Ser Leu Ala Arg
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                                                                      120
gctgcagact gactgcctga tgtccgtgcc cactggggtt tttccctttt cagaaaggat
                                                                      180
ttctccctga tctctcccca caaactctgg ctttgctttt tcatttccta agagcaactc
                                                                      240
aat atg cat ttc ccc atc caa gct acc ttc sac tat tcc cct act gat
                                                                      288
    Met His Phe Pro Ile Gln Ala Thr Phe Xaa Tyr Ser Pro Thr Asp
        -30
                            -25
tot etc tgt cat tta tat ttk tca etc tte tet tee ttt etc tge tet
                                                                      336
Ser Leu Cys His Leu Tyr Xaa Ser Leu Phe Ser Ser Phe Leu Cys Ser
    -15
                        -10
acc cct gcc cgg g
                                                                      349
Thr Pro Ala Arg
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                                                                       60
gggattccaa tccaagctct gggcca atg gct ttg cat atc cta gaa tgc gag
                                                                      113
                             Met Ala Leu His Ile Leu Glu Cys Glu
agg aac gtt tgt ttt gta gca gtt aga cag cct gct cat gaa agc tgc
                                                                      161
Arg Asn Val Cys Phe Val Ala Val Arg Gln Pro Ala His Glu Ser Cys
        -25
                            -20
ttt gtg ccc agc ctt gtg aca ggt gct tta caa caa tcc cag aca cag
                                                                      209
Phe Val Pro Ser Leu Val Thr Gly Ala Leu Gln Gln Ser Gln Thr Gln
                        -5
                                            1
cac cca cct tgg gtt tgc cct cag gta cag ggc tcc tat cca tcc tgg
                                                                      257
His Pro Pro Trp Val Cys Pro Gln Val Gln Gly Ser Tyr Pro Ser Trp
                10
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aag aac aga ggg a
Lys Asn Arg Gly
            25
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cag gtg ttg ttt tgt aat cga ag

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               Met Ser Tyr Phe Arg Cys Ile Phe Leu Ala Val Leu
                            -15
                                                -10
tca aaa atc agt tgg gct gta aat atg tgc agt ctt att tct ggg tcc
                                                                        97
Ser Lys Ile Ser Trp Ala Val Asn Met Cys Ser Leu Ile Ser Gly Ser
    -5
tcg gg
                                                                       102
Ser
<210> 457
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                                                                       55
                                       Met Leu Cys Ile Met Phe Gly
att gaa act aat gaa att acc aag atg aca atg tct ttt ctt ttg ttt
                                                                       103
Ile Glu Thr Asn Glu Ile Thr Lys Met Thr Met Ser Phe Leu Leu Phe
        -25
                             -20
                                                 -15
cta agt atc agt ttg ata act tta tat tcc tca gaa gca tgt ggg
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Leu Ser Ile Ser Leu Ile Thr Leu Tyr Tyr Ser Ser Glu Ala Cys Gly
    -10
                         -5
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40 45 50 caa gtg cca aca tac ggc cct tac ggc cgc tgt gcc ccc atg aag agc

Gln Val Pro Thr Tyr Gly Pro Tyr Gly Arg Cys Ala Pro Met Lys Ser 55 60 65 atc tcc agc agc ctc aag gag 311 Ile Ser Ser Ser Leu Lys Glu <210> 460 <211> 425 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 161..424 <221> sig_peptide <222> 161..418 <223> Von Heijne matrix score 4.59999990463257 seg AAAALCILILLXA/MY <400> 460 aggccgggct gatgcgcagg caatttatca tcttgatctc ccactgagtc agggagctct 60 cctgtcacca gtattgattt cagaggatgg actaaatttc ctaggatttc cattaagaat 120 taagaaaaaa gctctaagca cgcagggtag ccagacagac atg gat atg aga tgg 175 Met Asp Met Arg Trp -85 cac tgt gaa aac tcg cag acc aca gat gac atc ctt gtg gcc tca gca 223 His Cys Glu Asn Ser Gln Thr Thr Asp Asp Ile Leu Val Ala Ser Ala -80 -70 gag tgt ccc agc gat gat gag gac att gac ccc tgt gag ccg agc tca 271 Glu Cys Pro Ser Asp Asp Glu Asp Ile Asp Pro Cys Glu Pro Ser Ser -60 -55 ggt ggg tta gcc aac cca acc cga gca ggc ggc aga gag ccg tat cca 319 Gly Gly Leu Ala Asn Pro Thr Arg Ala Gly Gly Arg Glu Pro Tyr Pro -45 ggc tca gca gaa gtg atc cgg gag tcc agc agc acc acg ggt atg gtc 367 Gly Ser Ala Glu Val Ile Arg Glu Ser Ser Ser Thr Thr Gly Met Val -25 gtt ggg ata gta gcc gct gcc gcc ctg tgc atc ctt atc ctc ctc wat 415 Val Gly Ile Val Ala Ala Ala Leu Cys Ile Leu Ile Leu Leu Xaa -15 gcc atg tac a 425 Ala Met Tyr <210> 461 <211> 420 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 45..419 <221> sig_peptide <222> 45..104 <223> Von Heijne matrix score 4.59999990463257 seq PTLLTLCIGSVVS/SD

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cct	ctc	tgg	ccc	act	ctc	ctc	act	ctt	tac	ata	aat	_	gtg	att	tct	104
													Val			
tct	gac	ctg	act	cag	gac	cct	gct	gtg	tct	gtg	gcc	ttg	gga	cag	aga	152
Ser 1	Asp	Leu	Thr	Gln 5	Asp	Pro	Ala	Val	Ser 10	Val	Ala	Leu	Gly	Gln 15	Arg	
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			20					25				_	Phe 30			
tgg	tac	cga	cag	agg	ccc	gga	cag	gcc	cct	gtc	ctt	gtc	atc	tat	ggt	248
		35					40					45	Ile	•	-	
													ggc			296
	50					55				_	60		Gly		_	
tca	ggc	aat	aca	gct	tta	ttg	acc	atc	gyc	ggg	gct	cag	gcg	gag	gat	344
65					70					75			Ala		80	
gab	gct	gac	tat	tac	tgt	agt	kat	cgc	gac	cat	act	gat	aat	cgg	tgg '	392
Xaa	Ala	Asp	Tyr	Tyr 85	Cys	Ser	Xaa	Arg	Asp 90	His	Thr	Asp	Asn	Arg 95	Trp	
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Val	Phe	Gly	Gly 100	Gly	Thr	Arg	Leu	Thr 105					•			
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Phe	Tyr	Met	Xaa	Ile	Leu	Thr -10	Cys	Leu	Ile	Phe	Arg	aac Asn	tca Ser	gaa Glu	gly ggg	105
ttt		att	avc	cat '	atc		aaa	caa	cad	tat	-5 ctt	ttc	aaa	>>t	asa	153
Phe	Gln	Ile	Xaa	His 5	Val	Gln	Lys	Gln	Gln 10	Cys	Leu	Phe	Lys	Asn 15	Glu	133
	gtg	gtc	gtg	-	tca	tqc	aac	aqq		atc	cag	aac	cag		taa	201
Lys	Val	Val	Val 20	Gly	Ser	Cys	Asn	Arg 25	Thr	Ile	Gln	Asn	Gln 30	Gln	Trp	
atg	tgg	act		gat	gaa	aag	ctc		cat	gtt	aaa	tct	gca	cta	tac	249
Met	Trp	Thr 35	Glu	Asp	Glu	Lys	Leu 40	Leu	His	Val	Lys	Ser 45	Ala	Leu	Cys	
tta	gcc					_	4 V					43				257
Leu						-										~

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atg tgc gtg tgc gcg tgt gct ttg tgt gtg tgg ttg tgt gtt aaa tca
                                                                      108
Met Cys Val Cys Ala Cys Ala Leu Cys Val Trp Leu Cys Val Lys Ser
                            -10
tgc agt att
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Cys Ser Ile
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                                                                        56
                                          Met Ile Ser Asp Val Gln
                                               -20
cac ctt ttc ata tac ttg tta gcc ttt tgt atg cct tcc ttg gag aaa
                                                                      104
His Leu Phe Ile Tyr Leu Leu Ala Phe Cys Met Pro Ser Leu Glu Lys
                    -10
tgt cta tac ggg tct ttg gcc cac ttt ttt ttt ttt tt
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Cys Leu Tyr Gly Ser Leu Ala His Phe Phe Phe
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                                                                       120
aacttgagtg gctgcttttc tgggtggaaa agagcggtat cagacagggt gagcagtcgg
                                                                       180
ggaacggatg aacaaagact tgcaccgtgg ccctg atg cct ttg ttc cga gtt
                                                                       233
                                        Met Pro Leu Phe Arg Val
                                        -15
cta ttc agt tgw act tgt gcg ttg twa cag gac ttt aga atg cag ccc
                                                                       281
Leu Phe Ser Xaa Thr Cys Ala Leu Xaa Gln Asp Phe Arg Met Gln Pro
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tgc ccc cca acc ccc aag g
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Cys Pro Pro Thr Pro Lys
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Pro Val Leu	Val	Val	Ser	Phe	Val	Val	Gly	Gly	Leu	Gly	Cys	Asn	Xaa		
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Ala Pro Ile	Glu	Pro	Leu	Leu	Gln	Val	Leu	Arg	His	Asp	Gln	Gln	Gly		
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	Met
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Met Lys Phe Thr His Phe Lys	
att cgg tta tta tta cta tat tta cag aat cct gta acc atc	aca att 99
Ile Arg Leu Leu Leu Tyr Leu Gln Asn Pro Val Thr Ile	Thr Ile
-20 -15	-10
tta ttt tta atc gtt tcc atg gcc ctg aaa ata aac cac ata Leu Phe Leu Ile Val Ser Met Ala Leu Lys Ile Asn His Ile	
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ggg	150
Gly	·
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-	Ser Cys
atg tea ett tte eee tgt tge eet get eag agt aag aat tat	_
Met Ser Leu Phe Pro Cys Cys Pro Ala Gln Ser Lys Asn Ty	
-10 -5 1	5
tta tta ttc att att tta ctt cca act caa ttt tta tat tca	a aaa tta 331

Leu Leu Phe Ile Ile Leu Leu Pro Thr Gln Phe Leu Tyr Ser Lys Leu 10 15 gtt aca att tgc tgt tgt ttt 352 Val Thr Ile Cys Cys Cys Phe <210> 474 <211> 141 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 64..141 <221> sig_peptide <222> 64..105 <223> Von Heijne matrix score 4.5 seq LVCCTINSSFALG/IS <221> misc_feature <222> 38 <223> n=a, g, c or t <400> 474 tactttaagt tctagggtac gtctgcacaa cgtsrggntt tgatacatag gtatatatgt 60 gcc atg ttg gtt tgc tgc acc atc aac tca tca ttt gca tta ggt att 108 Met Leu Val Cys Cys Thr Ile Asn Ser Ser Phe Ala Leu Gly Ile -10 tct cgt aat gct atc cct ctg cca gcc cct ggg 141 Ser Arg Asn Ala Ile Pro Leu Pro Ala Pro Gly <210> 475 <211> 300 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 92..298 <221> sig peptide <222> 92..250 <223> Von Heijne matrix score 4.5 seq ALYVICQFILIRS/GV <400> 475 cagattaaga gatggagaaa ggtgtagggm tgattctttt tttggtgaga cctcgcataa 60 ctatcataaa tttgacagtg agtatgagag a atg gga cgt ggt cct ggc ccc 112 Met Gly Arg Gly Pro Gly Pro tta caa gag aga tct ctc ttt gag ama aag aga ggc gct cct cca agt 160 Leu Gln Glu Arg Ser Leu Phe Glu Xaa Lys Arg Gly Ala Pro Pro Ser -40 -35 age aat att gaa gae tte cat gga ete tta eeg aag gtt ate eec ate 208 Ser Asn Ile Glu Asp Phe His Gly Leu Leu Pro Lys Val Ile Pro Ile -30 -25 -20 -15 tgt gct cta tat gtg att tgc cag ttc att cta ata agg agt gga gtc 256 Cys Ala Leu Tyr Val Ile Cys Gln Phe Ile Leu Ile Arg Ser Gly Val

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cbn tcc ctc ttt ctc atc caa ttg ctt atc agc ttc tca gag aat ggt

Xaa Ser Leu Phe Leu Ile Gln Leu Leu Ile Ser Phe Ser Glu Asn Gly

1

-5

-10

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tatcrattaa tgtggtt atg tgt ggc ctg akk atc ctc tgt ggg cct tgg
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                   Met Cys Gly Leu Xaa Ile Leu Cys Gly Pro Trp
ctc cat gca gca cct cca tcc ccg ccg cgg g
                                                                      201
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                           Met Phe His Gly Arg Val Met Ala Met
                                        -30
ggt kat tta acc aaa cat tta aat cta aac att tct atc tca ctg ttg
                                                                       99
Gly Xaa Leu Thr Lys His Leu Asn Leu Asn Ile Ser Ile Ser Leu Leu
                -20
                                    -15
ctt atg ctg wwd gwa tat tgg tct tgt tgg ata aaa tca ccc ccg scc
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Leu Met Leu Xaa Xaa Tyr Trp Ser Cys Trp Ile Lys Ser Pro Pro Xaa
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Leu	Gly	Arg	Ser	Ser	Leu	Leu	Xaa	Trp	Lys	Xaa	Ser	Pro	Gly	Ser	Lys	
		-12	5				-12	0				-11	5		-	
aag	ttg	gtt	gta	gcc	aca	·gag	aag	aat	gtg	att	gca	gca	tta	aat	tcc	214
Lys	Leu	Val	Val	Ala	Thr	Glu	Lys	Asn	Val	Ile	Ala	Ala	Leu	Asn	Ser	
	-110					-10					-100	-				
cga	act	9 99	gag	atc	ttg	tgg	cgc	cat	gtt	gac	aag	ggc	acg	gca	gaa	262
Arg	Thr	Gly	Glu	Ile	Leu	Trp	Arg	His	Val	Asp	Lys	Gly	Thr	Ala	Glu	
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999	gct	gtg	gat	gcc	atg	ctg	ctg	cac	gga	cag	gat	gtg	atc	act	gtg	310
Gly	Ala	Val	Asp	Ala	Met	Leu	Leu	His	Gly	Gln	Asp	Val	Ile	Thr	Val	
				-75					-70					-65		
tcc	aat	gga	ggc	cga	atc	atg	cgt	tcc	tgg	gag	act	aac	atc	999	ggc	358
Ser	Asn	Gly	Gly	Arg	Ile	Met	Arg	Ser	Trp	Glu	Thr	Asn	Ile	Gly	Gly	
			-60					-55					-50			
ctg	aac	tgg	gag	ata	acc	ctg	gaç	agt	ggc	agt	ttc	cag	gca	ctt	ggg	406
Leu	Asn		Glu	Ile	Thr	Leu	Asp	Ser	Gly	Ser	Phe	Gln	Ala	Leu	Gly	
		-45		•			-40					-35				
ctg	gtt	ggc	ctg	cag	gag	tct	gta	agg	tac	atc	gca	gtc	ctg	aag	aag	454
Leu		Gly	Leu	Gln	Glu	Ser	Val	Arg	Tyr	Ile	Ala	Val	Leu	Lys	Lys	
	-30					-25					-20					
act	aca	ctt	gcc	ctc	cat	cac	ctc	tcc	agt	999	cac	tca	agt	ggg	tgg	502
Thr	Thr	Leu	Ala	Leu	His	His	Leu	Ser	Ser	Gly	His	Ser	Ser	Gly	Trp	
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260	
gtagtaggga aaagtgtcag ccctcgtgtc tggcactaag taccacccac cccaacccca gtgatgggag cctctaaatg actgagattt a atg tct act acc tat ttg aat Met Ser Thr Thr Tyr Leu Asn	180 232
-55	
gag gac ttg aag aag aaa ttc agt gca gtk ata gag cag gtg ctt ttt Glu Asp Leu Lys Lys Phe Ser Ala Val Ile Glu Gln Val Leu Phe -50 -45 -40 -35	280
gca cac tta tcc cca cta cat gtg tgg ctc cag ctc agg tct ctc tgt	328
Ala His Leu Ser Pro Leu His Val Trp Leu Gln Leu Arg Ser Leu Cys -30 -25 -20	320
gag trt ttg acc tgc atc tgg gtt aga ttc aat ttt tta gcc tca agc Glu Xaa Leu Thr Cys Ile Trp Val Arg Phe Asn Phe Leu Ala Ser Ser -15 -10 -5	376
caa gca tgc tcc aaa tgc aac tcc tcg ttt ctc atc atg tca tcc tct	424
Gln Ala Cys Ser Lys Cys Asn Ser Ser Phe Leu Ile Met Ser Ser Ser 1 5 10	
tca cc	429
Ser 15	
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cctcgaaaag gtccctcgct gtgg atg gca ctt atc gtt cta cag cta aca	171
Met Ala Leu Ile Val Leu Gln Leu Thr	
-35	
The Clarific Clarific War Vel When You I are Clarific Via Care I a The Clarific Control of the Care I are Care	219
Phe Gly Ile Gly Tyr Val Thr Leu Leu Gln Ile His Ser Ile Tyr Ser -30 -25 -20 -15	
-30 -25 -20 -15 caa tta att att ttg gat ctc ttg gtt cct gta ata ggc tta atc aca	262
Gln Leu Ile Ile Leu Asp Leu Leu Val Pro Val Ile Gly Leu Ile Thr	267
-10 -5	
gag cta cca tta cac atc aga gag act tta ctg ttt act tct tcc ttg	315
Glu Leu Pro Leu His Ile Arg Glu Thr Leu Leu Phe Thr Ser Ser Leu	313
5 10 15	
att ctc aca tta aat aca gtg ttt gtc ctg gca gtg aaa ctg aar tgg	363
Ile Leu Thr Leu Asn Thr Val Phe Val Leu Ala Val Lys Leu Lys Trp	
20 25 30	
ttt tat tat tcc aca cga tat g	385
Phe Tyr Tyr Ser Thr Arg Tyr	
35 40	
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                                                                       120
aggactecaa taataaccaa gteaatggee ttagtggaaa tacaacaatt cegtttagea
                                                                       180
gctgttgggc caactacaca gaccttactc cccttagaac aggaaaaaat tataagattg
                                                                       240
aatttatact ggataatgtt gttggggtag aatccagaac tttcagcctg ctggcagagt
                                                                       300
ctgtctctag cagtggcagc agcagcagca gcmacagcaa agcatcaact gtgggtacat
                                                                       360
atgeccagat a atg act gtm gta att age tgt etg gtt gga gaa tgt gge
              Met Thr Val Val Ile Ser Cys Leu Val Gly Glu Cys Gly
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Ser Trp Lys
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          Met Cys Thr Leu Thr Asp Thr His Thr His Val Gln Val His
                   ~45
                                       -40
aag toa aaa oot tgo cag oto oto too oot oot ooa ooa rso cat ggt
                                                                        99
Lys Ser Lys Pro Cys Gln Leu Leu Ser Pro Pro Pro Yaa His Gly
                                 -25
cct ctt ctc ccc atc ttt ggc ctt ctt gtg ccc tct cag att ttc
                                                                      147
Pro Leu Leu Pro Ile Phe Gly Leu Leu Val Pro Ser Gln Ile Phe
        -15
                             -10
ago tot ott otc aat tot ota cat otg ggo otg oot too tto oca aag
                                                                      195
Ser Ser Leu Leu Asn Ser Leu His Leu Gly Leu Pro Ser Phe Pro Lys
                                         10
                                                             15
atg cca ctc atg att ttc ctc ccc cgc tgg g
                                                                      226
Met Pro Leu Met Ile Phe Leu Pro Arg Trp
                 20
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                                                                       120
tgtcgcttgc gttcagctgt tctacaca atg gac tca gta cct gcc act gtg
                                                                       172
                               Met Asp Ser Val Pro Ala Thr Val
cct tct atc gcc gct acc ccg ggg gac ccg gaa ctt gtg gga ccc ttg
                                                                       220
Pro Ser Ile Ala Ala Thr Pro Gly Asp Pro Glu Leu Val Gly Pro Leu
                    -35
                                         -30
tot gtg ctc tac gca gcc ttc ata gcc aag ctg ctg gag cta gtt gct
                                                                       268
Ser Val Leu Tyr Ala Ala Phe Ile Ala Lys Leu Leu Glu Leu Val Ala
                -20
                                    -15
aca ttg cct gat gat gtt cag cct ggg cct gat ttt tat ggr stg sca
                                                                       316
Thr Leu Pro Asp Asp Val Gln Pro Gly Pro Asp Phe Tyr Gly Xaa Xaa
tgg aaa ctg tat tta tca ctg cct tct tgg gaa tkg ttc gtt tgc cat
                                                                      364
Trp Lys Leu Tyr Leu Ser Leu Pro Ser Trp Glu Xaa Phe Val Cys His
    10
ttt ctt atg gag act gtc ctt gtt gtg aag gnt aga gta tat cwa gtc
                                                                      412
Phe Leu Met Glu Thr Val Leu Val Val Lys Xaa Arg Val Tyr Xaa Val
                    30
                                        35
ac
                                                                      414
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gatetece atg gee geg tat the gee gha tgg gee teg ghe geg agt eee
                                                                      110
         Met Ala Ala Tyr Phe Ala Val Trp Ala Ser Val Ala Ser Pro
                     -15
                                         -10
gca tcc atc tgt tgc ggr amy tgg ctc aca ggg ctg gtg cgg cac gaa
                                                                      158
Ala Ser Ile Cys Cys Gly Xaa Trp Leu Thr Gly Leu Val Arg His Glu
                1
                                5
cgc atc gag gca cca tgg gcg cgt ggg
                                                                      185
Arg Ile Glu Ala Pro Trp Ala Arg Gly
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gctgcatgct ttcactttta ttagtactta cagccaaaga gatgggcaaa tgtctagaaa
                                                                      180
aattaatgtt ttgattcagg aatttgtgcc tagtgatggc ctccaataga gaattttcca
                                                                      240
gagaga atg aag act cag ttt cta agt tgg ggc aaa ttt agt ttt tgt
                                                                      288
       Met Lys Thr Gln Phe Leu Ser Trp Gly Lys Phe Ser Phe Cys
                       -25
ttt ggt att ctt ctt ata tta cag cta tta aaa bnn tct ctt aaa aaa
                                                                      336
Phe Gly Ile Leu Leu Ile Leu Gln Leu Lys Xaa Ser Leu Lys Lys
-15
                    -10
tgc cgg cac ggg
                                                                      348
Cys Arg His Gly
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     Met Leu Pro Ala Val Ala Val Ser Glu Pro Val Val Leu Arg Phe
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att ctg ccg agt tcc tgg gat tgc agg tgc gcg ccg cca ctc ctg act
                                                                       97
Ile Leu Pro Ser Ser Trp Asp Cys Arg Cys Ala Pro Pro Leu Leu Thr
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Gly Phe Cys Ile Phe Trp Xaa Glu Thr
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WO 99/53051 PCT/IB99/00712 266 <213> Homo sapiens <220> <221> CDS <222> 119..298 <221> sig_peptide <222> 119..217 <223> Von Heijne matrix score 4.40000009536743 seq WLLMVAPRLPAGA/RD <400> 493 acactgcctg cctggtgcag cccatgtgac gggtcgagct ccgggccctg ctgtccctgq 60 coggetate coagtogett caggeacett etecagaeet acceagaaag atgecogg 118 atg gat cct gca gct ccg tgg ctt ttc tgg gaa gca gcg gcc cct gct 166 Met Asp Pro Ala Ala Pro Trp Leu Phe Trp Glu Ala Ala Ala Pro Ala -30 -25 ctc aag aga ccc tgg ctc ctg atg gtg gcc cca agg ttg cca gct gqt 214 Leu Lys Arg Pro Trp Leu Leu Met Val Ala Pro Arg Leu Pro Ala Gly -15 -10 gct agg gac tca gga cag ttt ccc aga aaa ggc caa gcg ggc agc ccc 262 Ala Arg Asp Ser Gly Gln Phe Pro Arg Lys Gly Gln Ala Gly Ser Pro tcc agg ggc cgg gtg agg aag ctg ggg ggt gcg gtg gg 300

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cyc gcc tgg ctg cag ccc agg tat agg aag aat gcg tat ctt ttc atc Xaa Ala Trp Leu Gln Pro Arg Tyr Arg Lys Asn Ala Tyr Leu Phe Ile -100 -95 -90
tat tac tta atc cag ttc tgt ggc cas tct tgg ata ttt gca aat atg Tyr Tyr Leu Ile Gln Phe Cys Gly Xaa Ser Trp Ile Phe Ala Asn Met -85 -80 -75 -70
aca gtc aga ttc ttt tca ttt gga aaa gat tca atg gtt gac act ttt Thr Val Arg Phe Phe Ser Phe Gly Lys Asp Ser Met Val Asp Thr Phe -65 -60 -55
tat gct att gga ctt gtg atg cga ctt tgc caa tcc gta tct ctc ctg Tyr Ala Ile Gly Leu Val Met Arg Leu Cys Gln Ser Val Ser Leu Leu -50 -45 -40
gaa ctg ctg cac ata tat gtt ggc att gag tca aac cat ctt ctc cca Glu Leu Leu His Ile Tyr Val Gly Ile Glu Ser Asn His Leu Leu Pro -35 -30 -25
agg ttt ttg cag ctc aca gaa aga ata atc atc ctt ttt gtg gtg atc Arg Phe Leu Gln Leu Thr Glu Arg Ile Ile Leu Phe Val Val Ile -20 -15 -10
acc agt cga aga gga agt cca acg aga aat atg tgg tgt gtg tgt tat Thr Ser Arg Arg Gly Ser Pro Thr Arg Asn Met Trp Cys Val Cys Tyr -5 1 5 10
tcg tct ttg gat cta tgg ata tgg tta rgt aca ctt ata gca tgk tda Ser Ser Leu Asp Leu Trp Ile Trp Leu Xaa Thr Leu Ile Ala Xaa Xaa 15 20 25
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gac aca ttc cct tct ctt acc ctg act gcc tta ttg gtg cct agt aga Asp Thr Phe Pro Ser Leu Thr Leu Thr Ala Leu Leu Val Pro Ser Arg -15 -10 -5
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                                                                       120
ggttgctagg gctgggggaa ctcagattgc ttcacctgtg gtatcagaca tcacaac
                                                                       177
atg ggg ctc acc aag cag tac cta cgc tat gtt gct agt gcg gtc ttt
                                                                       225
Met Gly Leu Thr Lys Gln Tyr Leu Arg Tyr Val Ala Ser Ala Val Phe
-20
                                         -10
ggc gtt atc ggc agc caa aaa ggt aat att gtc ttt gtg aca ctt cgt
                                                                       273
Gly Val Ile Gly Ser Gln Lys Gly Asn Ile Val Phe Val Thr Leu Arg
ggt gag aaa gga cgt tat gtg gca gta cca gct tgt gaa cac gtt ttc
                                                                     . 321
Gly Glu Lys Gly Arg Tyr Val Ala Val Pro Ala Cys Glu His Val Phe
atc wgg gac tta agg aaa gga gag aag att ctt atc ctt cag ggg ctt
                                                                      369
Ile Xaa Asp Leu Arg Lys Gly Glu Lys Ile Leu Ile Leu Gln Gly Leu
                        35
aaa caa gaa gtt act tgc tta tgc ccc tcc cca gat ggg cta cac tta
                                                                      417
Lys Gln Glu Val Thr Cys Leu Cys Pro Ser Pro Asp Gly Leu His Leu
45
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Ala Val Gly Tyr
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<222> 7,359
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                                                                      120
gragaageet egetgaatee cagecagetg gttetaacet tecagaateg caatecette
                                                                      180
tecceacage cagecetege egageaagea geaggatgtt tgeagtgteg egeceaggge
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271 tetgagactg ageetgeeat ceactegeac geetttett cagggetttt eggetgttgg ctacactgat gtgacccccc tecetttttg ga atg atg ggg atc ttt ttg gtg 353 Met Met Gly Ile Phe Leu Val tat gtn gga ttt gtt ttc ttt tcc gtt tta tat gta caa caa ggg ctt 401 Tyr Val Gly Phe Val Phe Phe Ser Val Leu Tyr Val Gln Gln Gly Leu -15 -10 tct tct caa gca 413 Ser Ser Gln Ala 1 <210> 503 <211> 167 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 26..166 <221> sig peptide <222> 26..91 <223> Von Heijne matrix score 4.40000009536743 seq WVLDPALLLTCLT/FP <400> 503 gaateggaca acttaaagte tegat atg age ete gga ttg cat teg aac tee 52 Met Ser Leu Gly Leu His Ser Asn Ser -20 tgg gtt cta gac cca gct ctg cta cta act tgt ctg acc ttc.ccc att 100 Trp Val Leu Asp Pro Ala Leu Leu Leu Thr Cys Leu Thr Phe Pro Ile -10 -5 tat aaa ctg ttg tgg gtg aga ggt ggg acw agg wga act ctr wgr gcv 148 Tyr Lys Leu Trp Val Arg Gly Gly Thr Arg Xaa Thr Leu Xaa Ala 10 ctg cac tcg gcg cgg acg g 167 Leu His Ser Ala Arg Thr <210> 504 <211> 420 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 217..420 <221> sig_peptide <222> 217..396 <223> Von Heijne matrix score 4.40000009536743 seq MWVXCXFCFVLFC/FE <221> misc_feature <222> 47..48,368..369,373 <223> n=a, g, c or t <400> 504 ggktccgctc cctggggcgc acgtcagtca ggaggcggaa gcgcagnnga ggcgggaagg

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									2	/2							
gat aat	tgta tgcc	agg act	agag ggac	gcgc	tc c	cggt	gtcc	t co	ggtc gaaa	atg	gca	gca	aac	: tct	ctgad tca		180 _. 234
				•						-60					-55	•	
Gly	Gln	Gly	Phe	Gln -50	Asn	Lys	Asn	Arg	Val -45	Ala	Ile	Leu	Ala	Glu -40			282
Thr	Lys	Arg	Lys -35	Glu	Asn	Tyr	Leu	Cys -30	Arg	Thr	Ser	Leu	Gln -25	Gln	atc Ile		330
Ile	Leu	Glu -20	Leu	Gly	Ile	Asp	Thr -15	Ile	Met	Trp	Val	Xaa -10	Cys	Xaa	ttt Phe		378
tgt Cys	ttt Phe -5	gtt Val	ttg Leu	ttt Phe	tgt Cys	ttt Phe 1	gag	acg Thr	gag Glu	tct Ser 5	cgc Arg	cct Pro	gto Val				420
<21	0 > 5 1 > 4 2 > D	57								,				· · .			
			sapi	ens								٠.					
	1 > C	DS 34	56														
<222	2 > 4	31	eptio 47 eijno														
	S	core	4:40 APLL	0000	0095	3674	3										
<222	2 > 4	16	featı 417 g, c		t											٠	
			_														
)> 50 gtcgg		agtto	ggcg	gg tọ	ggtt	gagt	g ga	agcg	gtcg	i		tcc (54
agc Ser	gcg Ala -30	aca Thr	cat His	cct	gga Gly	gct Ala -25	ggc Gly	ggg Gly	cgc Arg	cgc Arg	aqc	aaa	tgg Trp	gac Asp	caa Gln		102
cca Pro -15	gct Ala	cca Pro	gcc Ala	cca Pro	ctt Leu -10	ctc Leu	ttc Phe	ctc Leu	ccg Pro	cca Pro -5	gcg Ala	gcc Ala	cca Pro	ggt Gly	999 Gly 1		150
gag Glu	gtc Val	acc Thr	agc Ser 5	agt Ser	999 Gly	gga Gly	agt Ser	cct Pro 10	ggg Gly	gsc Xaa	acc Thr	aca Thr	gct Ala 15	gct Ala	cct Pro		198
Ser	Gly	Ala 20	Leu	Asp	Ala	Ala	Ala 25	Ala	Val	Ala	Ala	Lys 30	att Ile	Asn	Ala		246
Met	Leu 35	Met	Ala	Lys	Gly	Lys 40	Leu	Lys	Pro	Thr	Gln 45	Xaa	gct Ala	Ser	Glu		294
Lys 50	Leu	Gln	Ala	Pro	Gly 55	Lys	Gly	Leu	Thr	Ser 60	Asn	Lys	agc Ser	Lys	Asp 65		342
qaA	Leu	Val	Val	Ala 70	Glu	Val	Glu	Ile	Asn 75	Asp	Val	Pro		Thr 80	Cys		390
agg	aac	ttg	ctg	act	cga	gga	cag	ann	caa	gac	gag	atc	agc	cga	ctt		438

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cttctctccc ctgattgctc atg agt ccc ctt gat cag gct gta ata cgt gct
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                      Met Ser Pro Leu Asp Gln Ala Val Ile Arg Ala
gtg tgt ctc agt gga ggt tcc tgc tgg gga gga gtc cgt tgt ctt gtg
                                                                      221
Val Cys Leu Ser Gly Gly Ser Cys Trp Gly Gly Val Arg Cys Leu Val
-10
                    -5
cgt ggg ggc ccg aac ata ggc cct gca gcc cag ctg ctt ggg ggc att
                                                                      269
Arg Gly Gly Pro Asn Ile Gly Pro Ala Ala Gln Leu Leu Gly Gly Ile
cca ctc tgc tgg cca cca gct gtg act gca ggt gaa gtg aaa ctg c
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Pro Leu Cys Trp Pro Pro Ala Val Thr Ala Gly Glu Val Lys Leu
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<222> 201..202
<223> n=a, g, c or t
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                                                                      120
ttcctgcagt ccttttaagg aagaaaagtg a atg aac tca ttt cat ttt att
                                                                      172
                                   Met Asn Ser Phe His Phe Ile
                                   -15
                                                        -10
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WO 99/53051 PCT/IB99/00712 274 tss ttc ctc cct ttc ccc tgg gct gaa wnn gcg cag 208 Xaa Phe Leu Pro Phe Pro Trp Ala Glu Xaa Ala Gln <210> 508 <211> 169 <212> DNA, <213> Homo sapiens <220> <221> CDS <222> 65..169 <221> sig_peptide <222> 65..151 <223> Von Heijne matrix score 4.40000009536743 seq LLSTHTWTDTALA/FS. <400> 508 atacagacac ccagrsagga ccctgaacac acagacaggc acagggaccc ctgtqcccac 60 aggg atg ggc tgg cac tca cat agt tcc caa ggc gtg caw gca atg cct 109 Met Gly Trp His Ser His Ser Ser Gln Gly Val Xaa Ala Met Pro -25 -20 ctg ctg ctg tcc aca cac acc tgg aca gac aca gcc ctg gca ttc agc 157 Leu Leu Ser Thr His Thr Trp Thr Asp Thr Ala Leu Ala Phe Ser aca cac aca cac 169 Thr His Thr His <210> 509 <211> 118 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 12..116 <221> sig_peptide <222> 12..77 <223> Von Heijne matrix score 4.40000009536743 seq WFLRSWTWPQTAG/RV caattcaagt c atg crg gct gtg aga aac gcg ggg tcg tgg ttc ctg cgg 50 Met Xaa Ala Val Arg Asn Ala Gly Ser Trp Phe Leu Arg -20 -15 tcc tgg act tgg ccc cag aca gcc ggc agg gtc gtg gcc aga rsg ccg 98 Ser Trp Thr Trp Pro Gln Thr Ala Gly Arg Val Val Ala Arg Xaa Pro gcc ggg acc atc tgc aca gg 118 Ala Gly Thr Ile Cys Thr 10 <210> 510 <211> 402 <212> DNA

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actttccatt ctgagcccct ttaatccact tatacaatat aactactccc tgaattattt
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acacacacag ggaaatgcca cccaaatagc tct atg tgt gcc ttg ttc att ctt
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                                     Met Cys Ala Leu Phe Ile Leu
                                      -15
gtt tcc att tct ttg ttt tat gca ctt ttt atc tct cca tcc ata caa
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Val Ser Ile Ser Leu Phe Tyr Ala Leu Phe Ile Ser Pro Ser Ile Gln
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                                                                      120
tagcattgat agaggaagee cageetggtg tgeacage atg tae etg gtg tge aca
                                                                      176
                                          Met Tyr Leu Val Cys Thr
aca tgc acc tgg tgt gta ttt tct gaa atg ttt gtt cat gga tta aac
                                                                      224
Thr Cys Thr Trp Cys Val Phe Ser Glu Met Phe Val His Gly Leu Asn
        -45
                            -40
atc act cag ctc gtg ctg agc cag ctg gat tac ttt ttc cat tcc aat
                                                                      272
Ile Thr Gln Leu Val Leu Ser Gln Leu Asp Tyr Phe Phe His Ser Asn
                        -25
                                             -20
ctg aca aac ttg gtc ttg tat ttc tta gtc cat tta ctt ttt tcc ctt
                                                                      320
Leu Thr Asn Leu Val Leu Tyr Phe Leu Val His Leu Leu Phe Ser Leu
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age ctg ttt atg ccg ctg acg gg
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Ser Leu Phe Met Pro Leu Thr
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ggaagaaaaa gaaaacagga aagagaggag gcaacaggaa aatcggcctt cgtccttcag 180
tctacgcttg aaattgccag ggatggataa atctgaag atg aat gaa aaa aag aaa 236
Met Asn Glu Lys Lys Lys

-30 cta ctg gga acg gaa cag aaa caa aaa aaa agg atg gga aat ctg aag Leu Leu Gly Thr Glu Gln Lys Gln Lys Lys Arg Met Gly Asn Leu Lys -25 -20 ctg cta ttt ctt att ctg atc tta ata gca gga tac agg g 324 Leu Leu Phe Leu Ile Leu Ile Leu Ile Ala Gly Tyr Arg -5 <210> 514 <211> 303 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 212..301 <221> sig_peptide <222> 212..292 <223> Von Heijne matrix score 4.40000009536743 seq SALMLPLGCAVRT/RM <400> 514 tttccctcac tctctgcctc ccccatcgca ccccacagga gggtttccct cactctctgc 60 ctccccatc gcaacccaca ggagggtttc cctcactctg cctcctccaw cgcacccca 120 kggaggtgtt ttccctcact ggttctgttg gtggcggtgg cagcaatccg agtcacatgg 180 caccagagta tgtcacgggt ggcggatctg a atg ggg ctg cag agc ctc aca 232 Met Gly Leu Gln Ser Leu Thr -25 ctt cca gtg tct tgc agc cct tct gcc ctg atg ctt ccc ttg gga tgt 280 Leu Pro Val Ser Cys Ser Pro Ser Ala Leu Met Leu Pro Leu Gly Cys -15 -10 get gte ege acg ege atg ett ga 303 Ala Val Arg Thr Arg Met Leu 1 <210> 515 <211> 455 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 342..455 <221> sig peptide <222> 342..434 <223> Von Heijne matrix score 4.40000009536743 seq LTTLESLAGSVXS/EQ <400> 515 tcatatctgg waatggcaaa cagggatgaa aatcgattat gttttggaga ctccttttgg 60 acatgtatca gtgtgttgat ttgcacaaac caataaaagc cctacatttt ttggaaatgg 120 atcoctagat ttcaagcatg tataatcact caaagtggat atgatcacag gcattcttct 180 cttgagctca gcaaaactat gcctaccaac accgaagaga agtcaaagat ttttatgaaa 240 aaaaattgca gatgatgttg gtgagataat aggatatgag caatgaaccc ttgggtgggg 300 ttccagggca Cttaaattgc ctcgtgtctt gagtccttaa g atg gac tca aac aaa 356 Met Asp Ser Asn Lys -30 aaa tta gta tta tca ata aca ggt aat act gtg tgg att cta aca aca 404 Lys Leu Val Leu Ser Ile Thr Gly Asn Thr Val Trp Ile Leu Thr Thr

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-25
                         -20
                                              -15
tta gaa tca tta gct ggc agt gtc aam tct gaa caa gat ttg tca gct
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Tyr
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ggtgatattt ttgctcttat ttctkcaagt gaacttgaaa tcccaccctg ttggtttct
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cettetaaga etetg atg acg tgt atg tta gee tgt agg tgt agt ete amg
                                                                       231
                 Met Thr Cys Met Leu Ala Cys Arg Cys Ser Leu Xaa
                          -45
                                              -40
ggt ccc caa gat ttt cgt ttc tgc tct gtc ttt tct ctg ttg ctc aag
                                                                       279
Gly Pro Gln Asp Phe Arg Phe Cys Ser Val Phe Ser Leu Leu Lys
-35
                    -30
                                         -25
ttg ggt aat ttc tat ttt tct ttt wct dtc tgt ctw ttt ctw dta ctd
                                                                       327
Leu Gly Asn Phe Tyr Phe Ser Phe Xaa Xaa Cys Leu Phe Leu Xaa Leu
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                                     -10
wyn nnt tot gag atg gag tom cac tot tto ago
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Xaa Xaa Ser Glu Met Glu Ser His Ser Phe Ser
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accectegga aggeageeet geggteeett tgeegeeegt teeeteeegg ae atg qaq
                                                                       118
                                                           Met Glu
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seq IFLLYFKFWGTCA/ER

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            -60
                                 -55
acc aag aac tgg gag gtg gac gtg gcg gcc cag ctg ggc gag tat ctg
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Thr Lys Asn Trp Glu Val Asp Val Ala Ala Gln Leu Gly Glu Tyr Leu
                            -40
                                                 -35
gag gag ctg gat cag atc tgc att tct ttt gac gaa ggc aag acc aca
                                                                       262
Glu Glu Leu Asp Gln Ile Cys Ile Ser Phe Asp Glu Gly Lys Thr Thr
                        -25
                                             -20
atg aac ttc att gag gca gcg ttg ttg atc cat ggc tct gcc tgc gtc
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Met Asn Phe Ile Glu Ala Ala Leu Leu Ile His Gly Ser Ala Cys Val
                    -10
                                        -5
tac agt aag aag gtg gaa tac ctc tac tca ctc gtc tac cag gcc ctt
                                                                      358
Tyr Ser Lys Lys Val Glu Tyr Leu Tyr Ser Leu Val Tyr Gln Ala Leu
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gat ttc atc tct gga aag agg cgg gcc aag cag ctc tct tcg gtg cag
                                                                       406
Asp Phe Ile Ser Gly Lys Arg Arg Ala Lys Gln Leu Ser Ser Val Gln
gag gac agg gcc aat ggg gtt gca gct ccg ggg tcc cca gga ggc ag
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                                                                      120
ctgctagctg ttagcacttg gcagacggag ttctcctcta gggtagttct aactttgggt
                                                                      180
aata atg ttt gtc agc tac ctg ata tta aca ttg ctc cac gtt caa aca
                                                                      229
    Met Phe Val Ser Tyr Leu Ile Leu Thr Leu Leu His Val Gln Thr
qca qtq tta qca aqa c
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Ala Val Leu Ala Arg
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-25 -20	
ttc ttg ttt ttt tta ttc att ttt tta tta tac ttt aag ttc tgg ggt Phe Leu Phe Phe Leu Phe Ile Phe Leu Leu Tyr Phe Lys Phe Trp Gly	161
-15 -10 -5 aca tgt gca gaa cgt gca ggt ttg tta cat agg tat act cgt gcc atg Thr Cys Ala Glu Arg Ala Gly Leu Leu His Arg Tyr Thr Arg Ala Met 1 5 10	209
gag gtt tgc tgc acc cat caa cca tca tct aca tta ggt att tct cct Glu Val Cys Cys Thr His Gln Pro Ser Ser Thr Leu Gly Ile Ser Pro 15 20 25	257
aat gct ctc ctt ccc cta Asn Ala Leu Leu Pro Leu 30 35	275
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ccg cct ctg tgc atg cat ctg tcc atc cat ccc cky mtc tgt gca tgc Pro Pro Leu Cys Met His Leu Ser Ile His Pro Xaa Xaa Cys Ala Cys -15 -10 -5 1	162
atc tgt cca tcc atc cag gg Ile Cys Pro Ser Ile Gln 5	182
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Met Tyr Pro Arg	3
gtg tgg gga tgt ttt caa tta ctg cat ttn ctt can bga aca aga acs Val Trp Gly Cys Phe Gln Leu Leu His Xaa Leu Xaa Xaa Thr Arg Thr -30 -25 -20	
aca ggt aag tnw gtg tgt gtg Thr Gly Lys Xaa Val Cys -15 -10 -5	
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ggagacgcaa g atg gcg gct gtg gtg ctg gcg gcg acg cgg ttg ctg cgg  Met Ala Ala Val Val Leu Ala Ala Thr Arg Leu Leu Ar  -10 -5  ggc tcg ggt tct tgg ggc tgt tcg cgg ctg agg ttt gga cct cct gcg Gly Ser Gly Ser Trp Gly Cys Ser Arg Leu Arg Phe Gly Pro Pro Ala  1 5 10 15	g 98
ggagacgcaa g atg gcg gct gtg gtg ctg gcg gcg acg cgg ttg ctg cgg  Met Ala Ala Val Val Leu Ala Ala Thr Arg Leu Leu Ar  -10  -5  ggc tcg ggt tct tgg ggc tgt tcg cgg ctg agg ttt gga cct cct gcg Gly Ser Gly Ser Trp Gly Cys Ser Arg Leu Arg Phe Gly Pro Pro Ala  1  5  10  15  tac aga cgg ttt agt agt ggt ggt gcc tat ccc aac atc ccc ctc tct Tyr Arg Arg Phe Ser Ser Gly Gly Ala Tyr Pro Asn Ile Pro Leu Ser	98 98 a 146
ggagacgcaa g atg gcg gct gtg gtg ctg gcg gcg acg cgg ttg ctg cgg  Met Ala Ala Val Val Leu Ala Ala Thr Arg Leu Leu Ar  -10  -5  ggc tcg ggt tct tgg ggc tgt tcg cgg ctg agg ttt gga cct cct gcg Gly Ser Gly Ser Trp Gly Cys Ser Arg Leu Arg Phe Gly Pro Pro Ala  1  5  10  15  tac aga cgg ttt agt agt ggt ggt gcc tat ccc aac atc ccc ctc tct Tyr Arg Arg Phe Ser Ser Gly Gly Ala Tyr Pro Asn Ile Pro Leu Ser  20  25  30  tct ccc tta cct gga gta ccc aag cct gtt ttt gct aca gtt gat gga	98 98 146 146 194
ggagacgcaa g atg gcg gct gtg gtg ctg gcg gcg acg cgg ttg ctg ccg  Met Ala Ala Val Val Leu Ala Ala Thr Arg Leu Leu Arg  -10  -5  ggc tcg ggt tct tgg ggc tgt tcg cgg ctg agg ttt gga cct cct gcg Gly Ser Gly Ser Trp Gly Cys Ser Arg Leu Arg Phe Gly Pro Pro Ala  1  5  10  15  tac aga cgg ttt agt agt ggt ggt gcc tat ccc aac atc ccc ctc tct Tyr Arg Arg Phe Ser Ser Gly Gly Ala Tyr Pro Asn Ile Pro Leu Ser  20  25  30  tct ccc tta cct gga gta ccc aag cct gtt ttt gct aca gtt gat gga Ser Pro Leu Pro Gly Val Pro Lys Pro Val Phe Ala Thr Val Asp Gly 35	98 98 146 146 194
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ccgtctctga caaagggcac aca atg tac tgt ctg arg tgt gtg gag aaa ata
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                          Met Tyr Cys Leu Xaa Cys Val Glu Lys Ile
                           -25
                                               -20
gca aaa gct ctt tat ctc agc ctt aat tta tat ttt gca aat tca ctt
                                                                       401
Ala Lys Ala Leu Tyr Leu Ser Leu Asn Leu Tyr Phe Ala Asn Ser Leu
                    -10
                                         -5
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Tyr Tyr Met Cys Val Cys Ser Tyr Ile Tyr Phe Tyr Leu Xaa Ile Tyr
                                10
ktk tat kkt tta ata aaa ann dng tct tat tat gtt gcc cag act ggt
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Xaa Tyr Xaa Leu Ile Lys Xaa Xaa Ser Tyr Tyr Val Ala Gln Thr Gly
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                                                -20
agt gag gcg tcg gct gtg ttt ctc acc gcg gtc ttt tcc tcc cac tct
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Ser Glu Ala Ser Ala Val Phe Leu Thr Ala Val Phe Ser Ser His Ser
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tgg ctg gtt gga ccc cgc tat
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                                                                       120
gtgcggtgct gaaaaaaatg tatattctgt tgatttgggg tggagagttc tgtag atg
                                                                       178
tot gtt agg too act tgg tgc aga gct cag ttc aat tcc tgg gta tcc
                                                                       226
Ser Val Arg Ser Thr Trp Cys Arg Ala Gln Phe Asn Ser Trp Val Ser
-30
                    -25·
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Leu Leu Thr Phe Cys Leu Ile Asp Leu Ser Asn Val Asp Ser Gly Xaa
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                                                Met Val Ser Gly
gtt ccc tcg ggg ctg ggg aag agt gcg cgt ccc agg gga cgg cgg gcc
                                                                       162
Val Pro Ser Gly Leu Gly Lys Ser Ala Arg Pro Arg Gly Arg Arg Ala
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                                    -40
egg aaa cta ctg cct gca cct egg gce geg eec agg aca get eea gae
                                                                       210
Arg Lys Leu Leu Pro Ala Pro Arg Ala Ala Pro Arg Thr Ala Pro Asp
            -30
                                -25
tac ccc ggg ccc ctc cgg tta acc tgg ctt gtg gcg gcc ggg ctg gaa
                                                                       258
Tyr Pro Gly Pro Leu Arg Leu Thr Trp Leu Val Ala Ala Gly Leu Glu
                            -10
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                                                                       306
Gly Arg Val His Leu Ala Asp Thr Ser Ser Gly Arg Lys Thr Trp Pro
                                         10
ggg tgc ggc cat cag tgg aaa tgg aaa gcc ctc ttg atc cta gtg agg
                                                                       354
Gly Cys Gly His Gln Trp Lys Trp Lys Ala Leu Leu Ile Leu Val Arg
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Ala Phe Pro Ala
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                                                                       120
acttgggttt ttgggggtgt taggaggtag ggtggatgtt actattaaat acatttagac
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tttttaaaat aagtgtaact gatcatttcc aacaaatatt tactatgtcc atacttgtgc
                                                                       240
tecaaaagae aattetgtet teetettgag atacatgtet eggggeeeet gtaggtetgg
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tetgagaggg teece atg ggt gge tgt gte wge tgg ege ttt ett gga cae
                                                                       351
                 Met Gly Gly Cys Val Xaa Trp Arg Phe Leu Gly His
                     -30
                                          -25
tee tet get etc agg act gtg tgt age agt etg ege tea gya agg eca
                                                                       399
Ser Ser Ala Leu Arg Thr Val Cys Ser Ser Leu Arg Ser Xaa Arg Pro
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                                     -10
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Cys Trp Cys Asp Gly Leu Arg Leu Arg
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acaaaccgga cccgcaacca cc atg aac agc aaa ggt caa tat cca aca cag
                                                                      112
                         Met Asn Ser Lys Gly Gln Tyr Pro Thr Gln
                              -50
                                                  -45
cca acc tac cct gtg cag cct cct ggg aat tcc agt ata ccc tca gac
                                                                       160
Pro Thr Tyr Pro Val Gln Pro Pro Gly Asn Ser Ser Ile Pro Ser Asp
                        -35
                                             -30
ctt goa tot too toa ggo too acc eta tac ega tgo too acc tgo eta
                                                                       208
Leu Ala Ser Ser Ser Gly Ser Thr Leu Tyr Arg Cys Ser Thr Cys Leu
-25
                    -20
                                         -15
etc aga get eta teg tee gag ett tgt gea eec agg gge tge eac agt
                                                                      256
Leu Arg Ala Leu Ser Ser Glu Leu Cys Ala Pro Arg Gly Cys His Ser
                -5
                                    1
ccc cac cat gtc agc cgc att tcc tgg acc ctc tct gta tct tcc cat
                                                                      304
Pro His His Val Ser Arg Ile Ser Trp Thr Leu Ser Val Ser Ser His
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285 10 15 gge cca gtc tgt ggc tgt tgg gcc ttt agg ttc cac aat ccc cat qqc 352 Gly Pro Val Cys Gly Cys Trp Ala Phe Arg Phe His Asn Pro His Gly 30 tta tta tcc agt cgg tcc cat cta tcc amc tgg ctc cac agt gct ggt 400 Leu Leu Ser Ser Arg Ser His Leu Ser Xaa Trp Leu His Ser Ala Gly , 50 <210> 529 <211> 244 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 68..244 <221> sig_peptide <222> 68..133 <223> Von Heijne matrix score 4.30000019073486 seq LFFETGSPSVAQS/GV <400> 529 cttacagagt taataagcat caaagaactt actgaaggac tttataaatt aaataccatt atgtaga atg gtg gtg gtt agt gcc ttt att tat tta ttt ttt gag aca 109 Met Val Val Ser Ala Phe Ile Tyr Leu Phe Phe Glu Thr -20 -15 ggg tet ecc tet gte gee cag tet gga gtg cag tgg tgt gat ete gge 157 Gly Ser Pro Ser Val Ala Gln Ser Gly Val Gln Trp Cys Asp Leu Gly tta ctg cag cct ccg cct cct gga ttc aag cga ttc tct tgc ctc agc 205 Leu Leu Gln Pro Pro Pro Pro Gly Phe Lys Arg Phe Ser Cys Leu Ser 15 ctc cta ggt agb drg gat tgc aga cgt gcg cca ccc ggg 244 Leu Leu Gly Xaa Xaa Asp Cys Arg Arg Ala Pro Pro Gly 30 <210> 530 <211> 434. <212> DNA <213> Homo sapiens <220> <221> CDS <222> 124..432 <221> sig peptide <222> 124..195 <223> Von Heijne matrix score 4.30000019073486 seq LXFLGMFLSGMVA/QI <400> 530 ggsctttgga ttggawagag gagctgggca ggaggcaggg caaggagaaa gctgttcggg 60 ggtcttgtct ggattttggt tgcctcctcc aatgttcctc tacctctact acaaqqatqq 120 gtc atg ttt gtg tct gka aca rcg ttt ttc ttt kcg ctc ckc ttt ctg 168 Met Phe Val Ser Xaa Thr Xaa Phe Phe Phe Xaa Leu Xaa Phe Leu -20 -15 gge atg tte etc tet gge atg gtg get caa att gat get aac tgg aac Gly Met Phe Leu Ser Gly Met Val Ala Gln Ile Asp Ala Asn Trp Asn 1 ttc ctg gat ttt gcc tac cat ttt aca gta ttt gtc ttc tat ttt gga 264

Phe Leu Asp Phe Ala Tyr His Phe Thr Val Phe Val Phe Tyr Phe Gly gcc ttt tta ttg gaa gca gcc aca tcc ctg cat gat ttg cat tgc 312 Ala Phe Leu Leu Glu Ala Ala Thr Ser Leu His Asp Leu His Cys 30 aat aca acc ata acc rgg cag cca ctc ctg agt gat aac cag tat aac 360 Asn Thr Thr Ile Thr Xaa Gln Pro Leu Leu Ser Asp Asn Gln Tyr Asn 45 50 ata aac gta gca gcc tca att ttt gcc ttt atg acg aca gct tgt tat 408 Ile Asn Val Ala Ala Ser Ile Phe Ala Phe Met Thr Thr Ala Cys Tyr ggt tgc agt ttg ggt ctg gct tta cg 434 Gly Cys Ser Leu Gly Leu Ala Leu 75 <210> 531 <211> 406 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 284..406 <221> sig_peptide <222> 284..361 <223> Von Heijne matrix score 4.30000019073486 seq AXYLLVGLFPLKC/HX <221> misc feature <222> 384 · <223> n=a, g, c or t <400> 531 taatatatgt magaatagca gggaccatgt cttctgttca atatkgtatc ctgagcacct 60 agtatttaag taggtatttc agtaaataat gtaacatata taataaataa tattaatatt 120 tgttgactaa atgaatttag gtctggacct tgatggctta atgtctttct aaaaatctac 180 ttccatatct aagcetttet tgactaettt egeetttte tgtgaactta aaagtettta 240 ttcattgttt gccggatgct aaacatttac aaaagtaatc ctt atg tca tct gaa 295 Met Ser Ser Glu att ttc taw ktt dtk cak att gck tat gct tda tat ttg cta gtt ggt 343 Ile Phe Xaa Xaa Xaa Ile Ala Tyr Ala Xaa Tyr Leu Leu Val Gly -20 -15 ctt ttc cct cta aaa tgc cac wag agt hat ttt tct aag tna caa atc 391 Leu Phe Pro Leu Lys Cys His Xaa Ser Xaa Phe Ser Lys Xaa Gln Ile -5 tca tca ttt gtg gaa 406 Ser Ser Phe Val Glu <210> 532 <211> 212 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 23..211 <221> sig peptide

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ggg cgg ctg gcg tcc gcg tgc agc cac agc atc ctg aga cct tcg ggg Gly Arg Leu Ala Ser Ala Cys Ser His Ser Ile Leu Arg Pro Ser Gly -5 1 5	100
CCC gga gca gcc tcc ctt tgg tct gct tct cga agg ttc aat tca cag Pro Gly Ala Ala Ser Leu Trp Ser Ala Ser Arg Arg Phe Asn Ser Gln 10 15 20	148
agc act tca tat cta cca gga tat gtt cvt aaa aca tcc ctg agt tca Ser Thr Ser Tyr Leu Pro Gly Tyr Val Xaa Lys Thr Ser Leu Ser Ser 25 30 35 40	196
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ttt agc cag tat ttg gsy ytt tct aat cca gcc gcg gg Phe Ser Gln Tyr Leu Xaa Xaa Ser Asn Pro Ala Ala -5 1 5	149
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Leu Tr	gg acc rp Thr 25	Ser I	Phe (	Gln	Asn -20	Pro	Leu	Gln	Val	Val	Leu	Leu	Thr	Ser	287
Val Se -10	cc ctt er Leu	Xaa X	Kaa :	Xaa -5	Xaa	Xaa	Xaa	Gly	Ser 1	Val	Arg	Ile	Xaa 5	Leu	335
Ser H	ac tgg is Trp	Ser S	Ser :	Ser	Ala	Phe	Phe 15	Phe	Leu	att Ile	cwb Xaa	nck Xaa 20	kyw Xaa	hwt Xaa	383
	ca cat er His 25								aa						415
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gta ct Val Le	eu Lys	tgt g Cys V 5	tt t al I	ttt ( Phe	gta Val	Val	gct Ala 10	agt Ser	aat Asn	ggc Gly	Leu	ttc Phe 15	ttt Phe	cct Pro	158
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ctc ttt agt tta att aga tcc cat ttg tca att ttg gct ttt gtt gcc Leu Phe Ser Leu Ile Arg Ser His Leu Ser Ile Leu Ala Phe Val Ala -20 -15 -10 -5	281
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cttctgcact cacagccgaa ggaaagcagc aggttggggc ttcttgtggc caacttcag gcctgtcacc aggaaaggta agc atg gga gga agg aag atg gcg aca gat ga Met Gly Gly Arg Lys Met Ala Thr Asp Gl -65 -60  gaa aat gtc tat ggt tta gaa gag aac gct cag tcc cgg cag gag tcc Glu Asn Val Tyr Gly Leu Glu Glu Asn Ala Gln Ser Arg Gln Glu Ser -55 -40 acg cgg agg ctc atc ctt gtt ggg aga aca ggg gcc ggg aag agc gcc Thr Arg Arg Leu Ile Leu Val Gly Arg Thr Gly Ala Gly Lys Ser Ala -35 -25 act ggg aac agc atc ctg ggc cag aga cgg ttc ttc tcc agg ctg ggg Thr Gly Asn Ser Ile Leu Gly Gln Arg Arg Phe Phe Ser Arg Leu Gly -20 -15 -10 gcc acg tct gtg anc agg gcc tgc acc acg grh agc cgc agg tgg gac Ala Thr Ser Val Xaa Arg Ala Cys Thr Thr Xaa Ser Arg Arg Trp Asp -5 aag tgc cac gtg gaa gtc gtr gnd ctm gga cat vwk can nmn ggg aag Lys Cys His Val Glu Val Val Xaa Leu Gly His Xaa Xaa Xaa Gly Lys 10 25	a 113 u 161 209 257 305
cttctgcact cacagccgaa ggaaagcagc aggttggggc ttcttgtggc caacttcaggcctgtcacc aggaaaggta agc atg gga gga agg aag atg gcg aca gat ga Met Gly Gly Arg Lys Met Ala Thr Asp Gl -65 -60  gaa aat gtc tat ggt tta gaa gag aac gct cag tcc cgg cag gag tcc Glu Asn Val Tyr Gly Leu Glu Glu Asn Ala Gln Ser Arg Gln Glu Ser -55 -50 -45 -40  acg cgg agg ctc atc ctt gtt ggg aga aca ggg gcc ggg aag agc gcc Thr Arg Arg Leu Ile Leu Val Gly Arg Thr Gly Ala Gly Lys Ser Ala -35 -25  act ggg aac agc atc ctg ggc cag aga cgg ttc ttc tcc agg ctg ggg Thr Gly Asn Ser Ile Leu Gly Gln Arg Arg Phe Phe Ser Arg Leu Gly -20 -15 -10  gcc acg tct gtg anc agg gcc tgc acc acg grh agc cgc agg tgg gac Ala Thr Ser Val Xaa Arg Ala Cys Thr Thr Xaa Ser Arg Arg Trp Asp -5 1 5  aag tgc cac gtg gaa gtc gtr gnd ctm gga cat vwk can nmn ggg aag Lys Cys His Val Glu Val Val Xaa Leu Gly His Xaa Xaa Xaa Gly Lys 10 15 20 25  tgt cca aga cag atc ctg gct gtg agg aga gag gtc act gct a Cys Pro Arg Gln Ile Leu Ala Val Arg Arg Glu Val Thr Ala	a 113 u 161 209 257 305
Cttctgcact	a 113 u 161 209 257 305
Cttctgcact	a 113 u 161 209 257 305
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Cttctgcact	a 113 u 161 209 257 305

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                                                                        49
        Met Gln Leu Gln Val Leu Gly Arg Pro Gln Gly Ala Pro Gln
            -30
                                -25
ctg gct ccc cag gcc ttg gct cta act bnk acc ctc ctc cca gcc cca
                                                                        97
Leu Ala Pro Gln Ala Leu Ala Leu Thr Xaa Thr Leu Leu Pro Ala Pro
                            -10
gga gaa cac gat tck ccr atg stc att ggc cag ttt ccc cwa aac cct
                                                                       145
Gly Glu His Asp Ser Pro Met Xaa Ile Gly Gln Phe Pro Xaa Asn Pro
                                         10
ccc tcc gag cac ccg ggc gcc agt ccc agg cgg wmr ngg acg ggc tqq
                                                                       193
Pro Ser Glu His Pro Gly Ala Ser Pro Arg Arg Xaa Xaa Thr Gly Trp
                                    25
nra ccc caa agc tgg gac cgg agg gtg agc ccg gca gag gca gag aca
                                                                       241
Xaa Pro Gln Ser Trp Asp Arg Arg Val Ser Pro Ala Glu Ala Glu Thr
cgc agg
                                                                       247
Arg Arg
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ataccgagta gtgaaactgc caggtc atg gga gta tac acg tgt cca att ttt
                                                                      113
                             Met Gly Val Tyr Thr Cys Pro Ile Phe
                                 -40
gtg cat tac tac gag aac cat gga cca acc ccw agt ttc cnt gcc ttt
                                                                      161
Val His Tyr Tyr Glu Asn His Gly Pro Thr Pro Ser Phe Xaa Ala Phe
        -30
                            -25
att tcc ttt cat cta ttt act ttg ggc ttt ctt tgt tcc cta tgc ccc
                                                                      209
Ile Ser Phe His Leu Phe Thr Leu Gly Phe Leu Cys Ser Leu Cys Pro
    -15 '
                        -10
                                             - 5
cac ccc cac ggg
                                                                      221
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His Pro His Gly
1
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cgaaattcca gttgggcaaa aaacggctcc taccaaggtg ctcttcataa cgcctctgaa
                                                                      120
gaagccacag aacaaaacat acgagctggt acccaggcag ttttgcaggt ggatcacttt
                                                                      180
atggctattt ttaaaaaataa aataatcatt aaatatttct gttcagtatt tcagtataca
                                                                      240
gtatactttt cacaatataa aaatagaagc ttaatactqq qcattcatac tttttaaaqa
                                                                      300
gnatga atg aag aaa tog gtt too tgo tgt agt tot ota tgg gta agt
                                                                      348
       Met Lys Lys Ser Val Ser Cys Cys Ser Ser Leu Trp Val Ser
           -15
                                -10
ctt agt aaa gac gag aat gct gaa atg
                                                                      375
Leu Ser Lys Asp Glu Asn Ala Glu Met
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gcatgcgctt gatttcagat ccccattaca agctcataat gaatgagtca caggagaaag
                                                                      120
gtgrgacttg gggccctttc gtgcctgatg ggaagctcct gcmaccccgg ggagcccctc
                                                                      180
cagactgtcc ttgcccacct ggctgcactg gcctctttat gccaacccag tgaggacagg
                                                                      240
ttctgaggga cctggacag atg ctg ctc ccc cta gcc atg gct gga cga tgt
                                                                      292
                     Met Leu Leu Pro Leu Ala Met Ala Gly Arg Cys
                     -30
tat aca gcc aag cac agc acw gtg ctg ctc tca gga agc cca agg gct
                                                                      340
Tyr Thr Ala Lys His Ser Thr Val Leu Leu Ser Gly Ser Pro Arg Ala
                -15
                                    -10
gtg gtc agt gca gtg gtg atg gtg ggc aca ggg tgc
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                                                                        53
                                 Met Pro Ser Cys Cys Tyr Leu Arg
 get ttt etg etc tet gte eet etg ggg aaa gge tea gee ett aag gat
                                                                       101
 Ala Phe Leu Leu Ser Val Pro Leu Gly Lys Gly Ser Ala Leu Lys Asp
     -10
                         -5
 ccc gtg ct
                                                                       109
 Pro Val
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                                                                        47
   Met Val Ala Asp Lys Glu Val Gln Thr Arg Thr Leu Leu Ser
                    -20
 tca cta tgg ata gtc tgt tgc ctc cat cta gat tct ctt att tca rrr
                                                                        95
 Ser Leu Trp Ile Val Cys Cys Leu His Leu Asp Ser Leu Ile Ser Xaa
aaa tat cct ctc cat gca att agg aga tat tta tcg acg ctg aga aac
                                                                       143
Lys Tyr Pro Leu His Ala Ile Arg Arg Tyr Leu Ser Thr Leu Arg Asn
                             15
caa aga gcc gaa gaa cag gtt gca cgt ttt caa aaa ata cct aat ggt
                                                                       191
Gln Arg Ala Glu Glu Gln Val Ala Arg Phe Gln Lys Ile Pro Asn Gly
                         30
gaa aat gag aca atg att cct gta ttg aca tca aaa aaa gca agt gaa
                                                                       239
Glu Asn Glu Thr Met Ile Pro Val Leu Thr Ser Lys Lys Ala Ser Glu
                     45
                                         50
tta cca gtc agt gaa gtt gca agc att ctc caa gct gat ctt cag aat
                                                                       287
Leu Pro Val Ser Glu Val Ala Ser Ile Leu Gln Ala Asp Leu Gln Asn
                 60
                                     65
ggt cta aaa caa tgt gaa g
                                                                       306
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295
Gly Leu Lys Gln Cys Glu
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                                                                       60
 tttatttttt aataatgtaa tttttatt atg cat att tgt ctt ttt tct ,
                                                                       112
                                Met His Ile Cys Leu Phe Phe Ser
 ttt tct ttw wct ttt tkt ctt ttc ttt ttt ttt
                                                                       148
 Phe Ser Xaa Xaa Phe Xaa Leu Phe Phe Phe Phe
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ctggggttca gctgttgcaa aarkrattgg taataatgtc aagaaacttc agaaatttgc
                                                                      120
 ctccacagtc aagatgtggg tcttttraar aaamcrgkkr akkggcagra aactgacaga
                                                                      180
 catcataaat aatgaccatg aaaatgtaaa atatcttcct ggacacaagc tgccagaaa
                                                                      239
 atg tgg ttg cca tgt caa atc tta gcg agg ctg tgc agg atg cag acc
                                                                      287
 Met Trp Leu Pro Cys Gln Ile Leu Ala Arg Leu Cys Arg Met Gln Thr
                 -15
                                     -10
 tgc tgg tgt ttg tca ttc ccc acc agt tca ttc aca gaa tct gtg atg
 Cys Trp Cys Leu Ser Phe Pro Thr Ser Ser Phe Thr Glu Ser Val Met
 aga tca ctg gga gag tgc cca aga aag cgc tgg ggg ggg
                                                                      374
 Arg Ser Leu Gly Glu Cys Pro Arg Lys Arg Trp Gly Gly
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gag aag gga acc aag ccg cct tca gtt gag gat ggc ttc cag acc gtc Glu Lys Gly Thr Lys Pro Pro Ser Val Glu Asp Gly Phe Gln Thr Val -75 -60 -60	22
cct ctc atc act ccc ttg gag gtt aat cac tta cag ctg cct gct cca Pro Leu Ile Thr Pro Leu Glu Val Asn His Leu Gln Leu Pro Ala Pro -55 -50 -45	269
gaa aag gtg att gtg aag aca aga acg gaa tat cag ccg gaa cag aag Glu Lys Val Ile Val Lys Thr Arg Thr Glu Tyr Gln Pro Glu Gln Lys -40 -35	31
aac aaa ggg aag ttc cgg gtg cca aaa atc gct gaa ttt acg gtc acc Asn Lys Gly Lys Phe Arg Val Pro Lys Ile Ala Glu Phe Thr Val Thr -25 -20 -15	36
atc ctt gtc agc ctg gcc cta gct ttc ctt gcg tgc atc gtg ttc ctg  Ile Leu Val Ser Leu Ala Leu Ala Phe Leu Ala Cys Ile Val Phe Leu -10 -5 1 5	413
gtg gtt tac aaa gcc ttc acc tat gat cac agc tgc cca gag gat tcg Val Val Tyr Lys Ala Phe Thr Tyr Asp His Ser Cys Pro Glu Asp Ser 10 15 20	461
tct atr agc acc ggg Ser Xaa Ser Thr Gly 25	476
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ctc cta ttt tkc tgc atc tac tgg ggt caa tat gcc acc gat ggc att Leu Leu Phe Xaa Cys Ile Tyr Trp Gly Gln Tyr Ala Thr Asp Gly Ile -5 1 5	160
ggc aac gag agt gtg aag atc ttg gcc aag ctg ctc ttc tcc tcc agc Gly Asn Glu Ser Val Lys Ile Leu Ala Lys Leu Leu Phe Ser Ser Ser	208

297 ttc ctc atc ttc ctg ctg atg gg 231 Phe Leu Ile Phe Leu Leu Met 25 <210> 552 <211> 229 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 125..229 <221> sig_peptide -<222> 125..202 <223> Von Heijne matrix score 4.19999980926514 seq FLSFLSFFFFSFF/LF <400> 552 agtttcactc cgaaagtsct tcttacagag caactccaag gatgggctga aaagcacata 60 gagaaaatgg aacagtgcga agttggaagg tccgtgcggg tggcagcgcc agtgtgggga 120 tgag atg ctc aca gga cgg ttt tta ggc ggc tca caa ggg ttt ttt ctt 169 Met Leu Thr Gly Arg Phe Leu Gly Gly Ser Gln Gly Phe Phe Leu -20 -15 tet ttt ett tet tte ttt ttt tee ttt tte ett tte ett tte ett yet ttt 217 Ser Phe Leu Ser Phe Phe Phe Phe Ser Phe Phe Leu Phe Leu Xaa Phe -10 -5 ttt ttt ttt ttt 229 Phe Phe Phe Phe <210> 553 <211> 232 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 110..232 <221> sig_peptide <222> 110..193 <223> Von Heijne matrix score 4.19999980926514 seq FVFMSKLLLFSFS/FL <400> 553 acgatcagat ctgakragaa ttgagccccc aaaagcagtt atcagactat ttgaaataaa 60 gatttatatt cacctttaat aacaatgtac cattaataac acatattac atg ttt att 118 Met Phe Ile tkr taw rak atg aaa cag wcr ttt cat att ata gac ttt gtt ttc atg 166 Xaa Xaa Xaa Met Lys Gln Xaa Phe His Ile Ile Asp Phe Val Phe Met -20 agt aaa ctt tta tta ttt tca ttt tca ttt tta ara aaa gcr cgc atg 214 Ser Lys Leu Leu Phe Ser Phe Ser Phe Leu Xaa Lys Ala Arg Met awt aca gca gca cct ggg 232 Xaa Thr Ala Ala Pro Gly 10 <210> 554

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                                                                       180
gccagaagtc tttgaatgag gcatcaatgg atgaatattt aggcagctta gggctgtttc
gaaagctgac tgccaagg atg cct ctt gcc tct ttc ggg cca ttt cgg agc
                                                                       231
                   Met Pro Leu Ala Ser Phe Gly Pro Phe Arg Ser
                    -15
                                         -10
                                                                       279
agt tgt ttt gca gcc agg tcc atc att tgg aaa tca gga agg caa ggg
Ser Cys Phe Ala Ala Arg Ser Ile Ile Trp Lys Ser Gly Arg Gln Gly
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                                                                       120
gtattgaata attaccagct gttgttagtt atttgaaatt aggtgcctaa agcaacctct
                                                                       180
catcttgcag aaagtcatct ttcttgaaac tttttaaaaa cttgcttgaa ac atg gag
                                                                       238
                                                           Met Glu
                                                                       286
act tgg aat ggg acg tot atc ata gta gca cat ctg ara too tto toa
Thr Trp Asn Gly Thr Ser Ile Ile Val Ala His Leu Xaa Ser Phe Ser
                 -25
                                     -20
                                                                       334
ttc ctg ctg tca ttt ctg tcc ttt cgc agt cca ctt tgt cac cac ccc
Phe Leu Leu Ser Phe Leu Ser Phe Arg Ser Pro Leu Cys His His Pro
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Leu Gly
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ctc tcg ctc atc									344
Leu Ser Leu Ile	Pne Ala	ser cys	ser ser	1111 1		Leu	PIO	ьeu 5	
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aag agc agg gga Lys Ser Arg Gly agg agt ctg cgg Arg Ser Leu Arg -30 cca gat cac act Pro Asp His Thr -15 gtc ttc cct tct Val Phe Pro Ser 1 ccc atc tgc gtc Pro Ile Cys Val  <210> 560 <211> 328 <212> DNA <213> Homo sapic	ccc ckt Pro Xaa -45 gag tgg Glu Trp gta ctt Val Leu cag gtc Gln Val 5 atc tct Ile Ser	gtc cag Val Gln cct gat Pro Asp gct ctg Ala Leu -10 acc tgc Thr Cys caa ggt	act ctg Thr Leu -40 ctg tgc Leu Cys -25 gtg tgc Val Cys aga ctc Arg Leu gcc ttt Ala Phe	ggg c. Gly H tgc t. Cys L cac a. His S cca a. Pro A 10 cac g	g atg g Met V  at gct is Ala  tg agg eu Arg gc gca er Ala -5 gg aca trg Thr	tc a al T ggc Gly ctt Leu -20 tcc Ser ggg Gly cac His	aac Asn -35 ttt Phe atc Ile tca Ser cca	cca Ser 50 ctg Leu gtc Val tct Ser cat His 15 aat	114 162 210 258 306

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1

-15

-20

- 5

206

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302

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                                                 Met Gly Pro Val Pro Gly Ala Ala Ala Gly Val
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Xaa Pro Xaa Xaa Gly Glu Leu Ala Xaa Thr Leu Ser Leu Thr Cys Ser
                                    -15
                                                                                    -10
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 Val Ser Gly Val Ser Ile Thr Ser Tyr Tyr Trp Ser Trp Ile Arg Gln
 gcc cca ggg aag ggg ccg gag tgg atc ggg cdk atc gat cat agc ggg
                                                                                                                                                                256
Ala Pro Gly Lys Gly Pro Glu Trp Ile Gly Xaa Ile Asp His Ser Gly
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 gat acc gac tac aat ccc tcc ctc cag agt cga gtc acc ctc tca gtg
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 Asp Thr Asp Tyr Asn Pro Ser Leu Gln Ser Arg Val Thr Leu Ser Val
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 gac acg tcg aag aac cag ttc tca ctg agg ttg ctt tct gtg agc gca
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                                                                                                                                                                111
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seq LSLPSFLCTCCQF/FP

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                                                                      113
                             Met Ser Tyr Val Val Thr Lys Thr Lys
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Ala Ile Asn Gly Lys Tyr His Arg Phe Leu Gly Arg His Phe Pro Arg
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                                         -90
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Phe Tyr Val Leu Tyr Thr Ile Phe Met Lys Gly Leu Gln Met Leu Trp
                -80
                                     -75
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            -65
                                 -60
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306

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Met Thr Arg Arg Thr -20 -15 tet etg tgg tge tge age eet tet tee aga aca tee age tee etg tee Ser Leu Trp Cys Cys Ser Pro Ser Ser Arg Thr Ser Ser Ser Leu Ser	341
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ctt aac gag cat gct gcc ttc aag cat ctg ttt aac aaa gca cat ctt Leu Asn Glu His Ala Ala Phe Lys His Leu Phe Asn Lys Ala His Leu	226

308 gca cca ccc tta atc cat tta acb ctg agt gga cac agc aca tgt ttc 274 Ala Pro Pro Leu Ile His Leu Thr Leu Ser Gly His Ser Thr Cys Phe -10 -5 aga gag cac agg gtt ggg ggc aag gtc ata gat gaa cag cat ccc aag 322 Arg Glu His Arg Val Gly Gly Lys Val Ile Asp Glu Gln His Pro Lys 5 10 gca gaa gaa tot tto tta gta cag gag ggg 352 Ala Glu Glu Ser Phe Leu Val Gln Glu Gly <210> 574 <211> 121 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 35..121 <221> sig_peptide <222> 35..112 <223> Von Heijne matrix score 4.09999990463257 seq SLASFLLLTFLPS/LP <400> 574 accttectte teteettett teetteeete ette atg tet tte tet tee tet ete 55 Met Ser Phe Ser Ser Leu -25 cct cca tct ctc cct tcc ctc gct tcc ttc ctc ctt ttg acc ttc 103 Pro Pro Ser Leu Pro Pro Ser Leu Ala Ser Phe Leu Leu Thr Phe -15 -10 ctt cct tcc ctc cct cgg 121 Leu Pro Ser Leu Pro Arg 1 <210> 575 <211> 391 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 77..391 <221> sig_peptide <222> 77..214 <223> Von Heijne matrix score 4.09999990463257 seg GCAPLRWVPQIRG/CP <221> misc_feature <222> 31..32,314 <223> n=a, g, c or t <400> 575 aaaaactgts sagacttttg cccgtccatt nncrctatct ctccccactc tgggtgtcct 60 acceaaggeg etgtet atg egt gee eag gge etg tee tge gga tae eea get 112 Met Arg Ala Gln Gly Leu Ser Cys Gly Tyr Pro Ala -45 -40 cgc ccc ttg cag ccc ttt tta gag cat ctc gcg ggc tct ggc atc acc 160

Arg Pro Leu Gln Pro Phe Leu Glu His Leu Ala Gly Ser Gly Ile Thr

seq FXSCXCVSTLAYT/KG

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aagttteeta gta atg eee aag gat get gae etg get tte agt get tea	169
Met Pro Lys Asp Ala Asp Leu Ala Phe Ser Ala Ser -35	
-35 -30 ttg ttt gaa aga gca gag tcc ctt tat act ctg att tca aaa ttt ktt	217
Leu Phe Glu Arg Ala Glu Ser Leu Tyr Thr Leu Ile Ser Lys Phe Xaa	21/
-25 -20 -15	
tot tgt dtk tgt gtg tot acc ttg gca tat act aaa gga agg ggg gg	264
Ser Cys Xaa Cys Val Ser Thr Leu Ala Tyr Thr Lys Gly Arg Gly	201
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Met	
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Phe Val Asn Arg Thr Cys Phe Asn Ser Ser Phe Pro Ile Trp Met Pro	
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Met Xaa Gly Ser Ser Arg Xaa Xaa Gly	
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		-20				15				-10	
tta ttg ata Leu Leu Ile	Caa gat	CTC ac	t atg	tca	ccc a	ct gc	t gga	atg	cag	tgg	97
bed bed fie	-5	Deu III	r Mec	ser	Pro T	nr Al	a Gly	Met 5	Gin	Trp	
cat aat cat	-	cca ca	a gcc	ttq		gc cc	a ctq		abc	cc	144
His Asn His	Gly Pro	Pro Gl	n Ala	Leu	Pro C	ys Pr	o Leu	Arq	Xaa	-	
10			15			_	20	_			
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ccttgtttaa g	gac atc	aca gat	tgc	ctg	tat a	ac cc	agt	Met S -45 gtg	Ser E	Phe ccc	55 103
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ctc aat gtg Leu Asn Val	gac atc Asp Ile	aca gat Thr Asp ctg acc	tgc Cys -35 tgt	ctg Leu gac	tat a Tyr A ttc a	ac ccc sn Pro ta gat le Asp	agt Ser -30 ggt	Met S -45 gtg Val atc	tgt Cys tgc	ccc Pro	103
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ctc aat gtg Leu Asn Val -40 gtg gct cag Val Ala Gln -25 ggg tcg cct Gly Ser Pro -10 ggr atc aat Gly Ile Asn gtc ttg ggg	gac atc Asp Ile agc agt Ser Ser ttg gct Leu Ala rns cym Xaa Xaa 10 ctg agc	aca gai Thr Asp ctg acc Leu Thr -20 gag tgi Glu Cys -5 tgc ttt Cys Pho	tgc Cys -35 tgt Cys ctg ctg Leu	ctg Leu gac Asp ctt Leu tgt Cys	tat a Tyr A ttc a Phe I ggt g Gly X 1 ggt g Gly V	ac cccsn Protesta gat le Asp -1! na gwaaa Xaattg aagal Lys	agt Ser -30 ggt Gly a wkw	Met S -45 gtg Val atc Ile ksc Xaa gca Ala	tgt Cys tgc Cys att Ile 5	ccc Pro ttg Leu ttk Xaa	103 151 199
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ccttgtttaa g ctc aat gtg Leu Asn Val -40 gtg gct cag Val Ala Gln -25 ggg tcg cct Gly Ser Pro -10 ggr atc aat Gly Ile Asn gtc ttg ggg	gac atc Asp Ile agc agt Ser Ser ttg gct Leu Ala rns cym Xaa Xaa 10 ctg agc	aca gai Thr Asp ctg acc Leu Thr -20 gag tgi Glu Cys -5 tgc ttt Cys Pho	tgc Cys -35 tgt Cys ctg ctg Leu	ctg Leu gac Asp ctt Leu tgt Cys	tat a Tyr A ttc a Phe I ggt g Gly X 1 ggt g Gly V	ac cccsn Protesta gat le Asp -1! na gwaaa Xaattg aagal Lys	agt Ser -30 ggt Gly a wkw	Met S -45 gtg Val atc Ile ksc Xaa gca Ala	tgt Cys tgc Cys att Ile 5	ccc Pro ttg Leu ttk Xaa	103 151 199 247
ctc aat gtg Leu Asn Val -40 gtg gct cag Val Ala Gln -25 ggg tcg cct Gly Ser Pro -10 ggr atc aat Gly Ile Asn gtc ttg ggg Val Leu Gly 25	gac atc Asp Ile agc agt Ser Ser ttg gct Leu Ala rns cym Xaa Xaa 10 ctg agc	aca gai Thr Asp ctg acc Leu Thr -20 gag tgi Glu Cys -5 tgc ttt Cys Pho	tgc Cys -35 tgt Cys ctg ctg Leu ccg Pro	ctg Leu gac Asp ctt Leu tgt Cys	tat a Tyr A ttc a Phe I ggt g Gly X 1 ggt g Gly V	ac cccsn Protesta gat le Asp -1! na gwaaa Xaattg aagal Lys	agt Ser -30 ggt Gly a wkw	Met S -45 gtg Val atc Ile ksc Xaa gca Ala	tgt Cys tgc Cys att Ile 5	ccc Pro ttg Leu ttk Xaa	103 151 199 247
ccttgtttaa g ctc aat gtg Leu Asn Val -40 gtg gct cag Val Ala Gln -25 ggg tcg cct Gly Ser Pro -10 ggr atc aat Gly Ile Asn gtc ttg ggg Val Leu Gly	gac atc Asp Ile agc agt Ser Ser ttg gct Leu Ala rns cym Xaa Xaa 10 ctg agc	aca gai Thr Asp ctg acc Leu Thr -20 gag tgi Glu Cys -5 tgc ttt Cys Pho	tgc Cys -35 tgt Cys ctg ctg Leu ccg Pro	ctg Leu gac Asp ctt Leu tgt Cys	tat a Tyr A ttc a Phe I ggt g Gly X 1 ggt g Gly V	ac cccsn Protesta gat le Asp -1! na gwaaa Xaattg aagal Lys	agt Ser -30 ggt Gly a wkw	Met S -45 gtg Val atc Ile ksc Xaa gca Ala	tgt Cys tgc Cys att Ile 5	ccc Pro ttg Leu ttk Xaa	103 151 199 247
ccttgtttaa g ctc aat gtg Leu Asn Val	gac atc Asp Ile agc agt Ser Ser ttg gct Leu Ala rns cym Xaa Xaa 10 ctg agc	aca gai Thr Asp ctg acc Leu Thr -20 gag tgi Glu Cys -5 tgc ttt Cys Pho	tgc Cys -35 tgt Cys ctg ctg Leu ccg Pro	ctg Leu gac Asp ctt Leu tgt Cys	tat a Tyr A ttc a Phe I ggt g Gly X 1 ggt g Gly V	ac cccsn Protesta gat le Asp -1! na gwaaa Xaattg aagal Lys	agt Ser -30 ggt Gly a wkw	Met S -45 gtg Val atc Ile ksc Xaa gca Ala	tgt Cys tgc Cys att Ile 5	ccc Pro ttg Leu ttk Xaa	103 151 199 247
ccttgtttaa g ctc aat gtg Leu Asn Val -40 gtg gct cag Val Ala Gln -25 ggg tcg cct Gly Ser Pro -10 ggr atc aat Gly Ile Asn gtc ttg ggg Val Leu Gly 25 <210> 585 <211> 388	gac atc Asp Ile agc agt Ser Ser ttg gct Leu Ala rns cym Xaa Xaa 10 ctg agc Leu Ser	aca gai Thr Asp ctg acc Leu Thr -20 gag tgi Glu Cys -5 tgc ttt Cys Pho	tgc Cys -35 tgt Cys ctg ctg Leu ccg Pro	ctg Leu gac Asp ctt Leu tgt Cys	tat a Tyr A ttc a Phe I ggt g Gly X 1 ggt g Gly V	ac cccsn Protesta gat le Asp -1! na gwaaa Xaattg aagal Lys	agt Ser -30 ggt Gly a wkw	Met S -45 gtg Val atc Ile ksc Xaa gca Ala	tgt Cys tgc Cys att Ile 5	ccc Pro ttg Leu ttk Xaa	103 151 199 247
ctc aat gtg Leu Asn Val	gac atc Asp Ile agc agt Ser Ser ttg gct Leu Ala rns cym Xaa Xaa 10 ctg agc Leu Ser	aca gai Thr Asp ctg acc Leu Thr -20 gag tgi Glu Cys -5 tgc ttt Cys Pho	tgc Cys -35 tgt Cys ctg ctg Leu ccg Pro	ctg Leu gac Asp ctt Leu tgt Cys	tat a Tyr A ttc a Phe I ggt g Gly X 1 ggt g Gly V	ac cccsn Protesta gat le Asp -1! na gwaaa Xaattg aagal Lys	agt Ser -30 ggt Gly a wkw	Met S -45 gtg Val atc Ile ksc Xaa gca Ala	tgt Cys tgc Cys att Ile 5	ccc Pro ttg Leu ttk Xaa	103 151 199 247
ctc aat gtg Leu Asn Val	gac atc Asp Ile agc agt Ser Ser ttg gct Leu Ala rns cym Xaa Xaa 10 ctg agc Leu Ser	aca gai Thr Asp ctg acc Leu Thr -20 gag tgi Glu Cys -5 tgc ttt Cys Pho	tgc Cys -35 tgt Cys ctg ctg Leu ccg Pro	ctg Leu gac Asp ctt Leu tgt Cys	tat a Tyr A ttc a Phe I ggt g Gly X 1 ggt g Gly V	ac cccsn Protesta gat le Asp -1! na gwaaa Xaattg aagal Lys	agt Ser -30 ggt Gly a wkw	Met S -45 gtg Val atc Ile ksc Xaa gca Ala	tgt Cys tgc Cys att Ile 5	ccc Pro ttg Leu ttk Xaa	103 151 199 247
ctc aat gtg Leu Asn Val	gac atc Asp Ile agc agt Ser Ser ttg gct Leu Ala rns cym Xaa Xaa 10 ctg agc Leu Ser	aca gai Thr Asp ctg acc Leu Thr -20 gag tgi Glu Cys -5 tgc ttt Cys Pho	tgc Cys -35 tgt Cys ctg ctg Leu ccg Pro	ctg Leu gac Asp ctt Leu tgt Cys	tat a Tyr A ttc a Phe I ggt g Gly X 1 ggt g Gly V	ac cccsn Protesta gat le Asp -1! na gwaaa Xaattg aagal Lys	agt Ser -30 ggt Gly a wkw	Met S -45 gtg Val atc Ile ksc Xaa gca Ala	tgt Cys tgc Cys att Ile 5	ccc Pro ttg Leu ttk Xaa	103 151 199 247

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                                                                     60
aaatgtttga ggtgagggat atcccaatta ccctgatttg gttattattc attgtataca
gttttcaaaa tatcacatgt acccccaaaa tatgtaaaac tgttatatac aaataaataa
caaaactaaa aataacagct gtgcaaacat ttttaaaagg cttgctttaa atgggtttca
                                                                    240
c atg aaa gta gga aag gac tot otg gag tot tta oca tot tta tgt gag
                                                                    289
  Met Lys Val Gly Lys Asp Ser Leu Glu Ser Leu Pro Ser Leu Cys Glu
          ~35
                              -30
aaa cac att ggt ccc agt ggt ctc ttt acc ttt ctt agt cca tcc ttt
                                                                    337
Lys His Ile Gly Pro Ser Gly Leu Phe Thr Phe Leu Ser Pro Ser Phe
                        -15
cac tot gta cat ott tot gaa oto aat gaa tta tac act att got goo
                                                                    385
His Ser Val His Leu Ser Glu Leu Asn Glu Leu Tyr Thr Ile Ala Ala
ggg
                                                                    388
Gly
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<222> 346..396
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      seq VLISASLLRASQL/KI
<221> misc_feature
<222> 170
<223> n=a, g, c or t
<400> 586
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                                                                    120
ccaagttcag gggagagagt ttaaaggcgg gatgatcata tgtgaagdhn tggcagcacc
                                                                    180
aatatggcac tgtcaaagta aaagagaaat agatctgaac tggattttaa tgagaataat
                                                                    240
agcaaatatt aacatttett agatagtttg atatttatte tggaagtate getaccaaca
                                                                    300
tcaacatctg ggaaagcdag tgggcatcaa aatcctacct ggcta atg gaa agc aaa
                                                 Met Glu Ser Lys
gtt tta atc agt gca tca ctc cta cgg gcc tct caa tta aaa ata aaa'
                                                                    405
Val Leu Ile Ser Ala Ser Leu Leu Arg Ala Ser Gln Leu Lys Ile Lys
            -10
                               -5
tgr aac aaa atg aca aac ttc tta att ttg t
                                                                   436
Xaa Asn Lys Met Thr Asn Phe Leu Ile Leu
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<211> 378
<212> DNA
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<400> 587
teetgteetg ggegtaegte aag atg geg geg tet gta tta aac acc gtg etg
                                                                       53
                          Met Ala Ala Ser Val Leu Asn Thr Val Leu
                                           -20
agg cgg ctt cct atg cta tct ctc ttc cga ggt tct cay vvg rbg ttc
                                                                      101
Arg Arg Leu Pro Met Leu Ser Leu Phe Arg Gly Ser His Xaa Xaa Phe
                -10
                                    -5
agg ttc ccc tcc aga ctc ttt gca cca aag ctc cct ctg agg aag att
                                                                      149
Arg Phe Pro Ser Arg Leu Phe Ala Pro Lys Leu Pro Leu Arg Lys Ile
                            10
ctt tgt cct cag ttc cca ttt ctc ctt ata agg atg agc cct gga aat
                                                                      197
Leu Cys Pro Gln Phe Pro Phe Leu Leu Ile Arg Met Ser Pro Gly Asn
    20
                        25
atc tgg aat cag aag aat acc agg agc gat atg gtt ctc gcc ccg tct
                                                                      245
Ile Trp Asn Gln Lys Asn Thr Arg Ser Asp Met Val Leu Ala Pro Ser
                    40
                                         45
ggg ctg act acc gcc gca acc aca agg gtg gtg tac ccc cac agc gga
                                                                      293
Gly Leu Thr Thr Ala Ala Thr Thr Arg Val Val Tyr Pro His Ser Gly
                55
                                    60
ctc gga aga cat gta ttc gtc gga ata aag ttg ttg gga atc cct gcc
                                                                      341
Leu Gly Arg His Val Phe Val Gly Ile Lys Leu Leu Gly Ile Pro Ala
                                75
                                                                      378
cca tct gtc gag atc aca agt tgc atg ttg act tta g
Pro Ser Val Glu Ile Thr Ser Cys Met Leu Thr Leu
                            90
<210> 588 '
<211> 413
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<221> sig peptide
<222> 185..238
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      seq TLLTCLXLXGGEG/WK
<221> misc_feature
<222> 218,224
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cagecageca tgeeteeagt teaggtaett ggeattgeta ageteagaac aggaettgee
                                                                      120
agtgtetaga tgaaaaagag gagagatete aaqagggata accaattgge tggcaaagta
                                                                      180
acaa atg aaa agt aac ctg act cta ttg acc tgc tta nec ctg nat ggg
                                                                      229
     Met Lys Ser Asn Leu Thr Leu Leu Thr Cys Leu Xaa Leu Xaa Gly
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316 -10 ggg gaa gga tgg aaa gga gca gct gtt tgc ttt gaa acg gtg gaa cag 277 Gly Glu Gly Trp Lys Gly Ala Ala Val Cys Phe Glu Thr Val Glu Gln. ttt tgc agc ctt aga aaa tgg cat gta aca tac cta rcc aaa gac agc 325 Phe Cys Ser Leu Arg Lys Trp His Val Thr Tyr Leu Xaa Lys Asp Ser 20 gga ctc tgt caa caa cag gag aag ctc tat acg aaa ttc ttg gtc tgc 373 Gly Leu Cys Gln Gln Gln Glu Lys Leu Tyr Thr Lys Phe Leu Val Cys 35 40 ata aag gga gca tca aat gaa gaa att aag aaa acc tac a 413 Ile Lys Gly Ala Ser Asn Glu Glu Ile Lys Lys Thr Tyr 50 <210> 589 <211> 210 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 138..209 <221> sig_peptide <222> 138..179 <223> Von Heijne matrix score 4.09999990463257 seq LASPCVLVQGSGX/SL <221> misc_feature · <222> 78,80,118 <223> n=a, g, c or t <400> 589 gaagataata ataatgatta ttataataat gatgatgatt ccaaggaaaa aacctacagc 60 gaatgttcca tttctacnsn gcacgcagac actctcccta acactgataa cctqagcncc 120 cagcactgga cggaaga atg ctg gcg tct ccg tgt gta ctg gtt cag ggt 170 Met Leu Ala Ser Pro Cys Val Leu Val Gln Gly -10 tct ggs bcc agc ctt gtc agg acc ccc tgg tgt cca gag c 210 Ser Gly Xaa Ser Leu Val Arg Thr Pro Trp Cys Pro Glu <210> 590 <211> 178 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 40..177 <221> sig_peptide . <222> 40..96 <223> Von Heijne matrix score 4.09999990463257 seq ILLLITIIYSYL/ES <400> 590 acaaggactg aaccagaagg aagaggacag agcaaagcc atq aac atc atc cta 54

Met Asn Ile Ile Leu

317

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gaa atc ctt ctg ctt ctg atc acc atc atc tac tcc tac ttg gag tcg
Glu Ile Leu Leu Leu Ile Thr Ile Ile Tyr Ser Tyr Leu Glu Ser
                -10
                                     -5
ttg gtg aag ttt ttc att cct cag agg aga aaa tct gtg gct ggg gag
                                                                       150
Leu Val Lys Phe Phe Ile Pro Gln Arg Arg Lys Ser Val Ala Gly Glu
                            10
att gtt ctc att act gga gct ggg cat g
                                                                       178
Ile Val Leu Ile Thr Gly Ala Gly His
    20
<210> 591
<211> 308
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<221> CDS
<222> 149..307
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<222> 149..265
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      seq PSLIAGLFVGCLA/GY
<221> misc_feature
<222> 272
<223> n=a, g, c or t
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                                                                       60
gtaccgcgct tggccgcagc tggccccaga cttctgtctt ttcaagmkgc aagtraargc
                                                                      120
tcggggctgc rraattgcaa ccttgcca atg gac ctg atc ggt ttt ggt tat
                                                                      172
                               Met Asp Leu Ile Gly Phe Gly Tyr
                                                -35
gca gcc ctc gtg aca ttt gga agc att ttt gga tat aag cdg aga ggt
                                                                      220
Ala Ala Leu Val Thr Phe Gly Ser Ile Phe Gly Tyr Lys Xaa Arg Gly
                        -25
ggt gtt ccg tct ttg att gct ggt ctt ttt gtd gga tgt ttg gcc ggc
                                                                      268
Gly Val Pro Ser Leu Ile Ala Gly Leu Phe Val Gly Cys Leu Ala Gly
                    -10
                                        -5
tat nsa gct tac cgt gtc tcc aat gac aaa cga gat gta a
                                                                      308
Tyr Xaa Ala Tyr Arg Val Ser Asn Asp Lys Arg Asp Val
<210> 592
<211> 219
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<220>
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<221> sig peptide
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      score 4.09999990463257
      seq XTFLAAXRRLVTG/QT
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Met Glu Gly Val Ala Xaa Xaa Thr Phe Leu Ala Ala -15 -10	
sgg cgg cgg ttg gta acc ggt cag acc agc ccg aga ggg acc tgg tgc	, 99
Xaa Arg Arg Leu Val Thr Gly Gln Thr Ser Pro Arg Gly Thr Trp Cys  -5  1  5	23
ctg tac cca ggc ttc tgt cgc tct gtc gcc tgc gct atg ccc tgc tgt	147
Leu Tyr Pro Gly Phe Cys Arg Ser Val Ala Cys Ala Met Pro Cys Cys 10 20 25	
agt cac agg agc tgt aga gag gac ccc ggt aca tct gaa agc cgg gaa	195
Ser His Arg Ser Cys Arg Glu Asp Pro Gly Thr Ser Glu Ser Arg Glu 30 35 40	
atg gtg cgt gtg cgg gac cac ggg	219
Met Val Arg Val Arg Asp His Gly 45	
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gtactgtott agtotgtttt tatgotgotg ataacgacat accc atg act ggg caa Met Thr Gly Gln	116
-20	
ttt aca aaa gaa ata ggt tta att gga ctt aca gtt cca tgt ggc tgg	164
Phe Thr Lys Glu Ile Gly Leu Ile Gly Leu Thr Val Pro Cys Gly Trp	
-15 -10 -5 gga agc ctc ata acc atg gca gaa ggc agg gag gag caa gtc acg tct	212
Gly Ser Leu Ile Thr Met Ala Glu Gly Arg Glu Glu Gln Val Thr Ser	212
1 5 10 15	
ggg Gly	215
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score 4	
seq HLGFILSFHGLIA/NF	
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ttcacattgg cttctttcac taaataac atg cat tta gga ttc att ctt tct	112
Met His Leu Gly Phe Ile Leu Ser	

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-10
ttc cat ggt ttg ata gct aat ttc ttt ttt tgt ctg aat gca cca gcg g
                                                                       161
Phe His Gly Leu Ile Ala Asn Phe Phe Phe Cys Leu Asn Ala Pro Ala
<210> 595
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<222> 317..394
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<222> 317..376
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<222> 149
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                                                                      120
tecetgeaga tettggggee ggaggeagnt ceaaccettg gageaggaag aaacgeaaag
                                                                      180
ttgtcaagaa ccaagtcgag ctgcctcaga gccggcccgc agtagctgca gactccqccc
                                                                      240
gegacgtgtg egegettete tgggccagag egageetgtt ttgtgetegg qttaagagat
                                                                      300
ttgtccbagc tatacc atg ggc cgc act cgg gaa gct ggc tgc gtg gcc gct
                                                                      352
                  Met Gly Arg Thr Arg Glu Ala Gly Cys Val Ala Ala
                                      -15
ggt gtg gtt atc ggg gct ggt gct gct act gtg tat aca gac tg
                                                                      396
Gly Val Val Ile Gly Ala Gly Ala Ala Thr Val Tyr Thr Asp
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<222> 228..407
<221> sig_peptide
<222> 228..341
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caaatatttt ctcactctgg gtaggttgtc tttttacttt cttgataatg tcctcttttg
                                                                      120
ttgcttgtgt tatctccttt tttgtttttt attctttta aagttatctc ttacaggaag
                                                                      180
gattcctttt ttcttaaaaa agtttttcaa ttctttttt ttttgag atg gag tct
                                                                      236
                                                    Met Glu Ser
cac tot gto gco cag gct agg atg cgg ysg caw aat oto ago toa otg
                                                                      284
His Ser Val Ala Gln Ala Arg Met Arg Xaa Xaa Asn Leu Ser Ser Leu
                    -30
                                        -25
caa cct ctg ccg cct ggg ttc aag cca tts tcc tgc ctm agc ctc ctg
                                                                      332
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320

Gln Pro Leu Pro Pro Gly Phe Lys Pro Xaa Ser Cys Leu Ser Leu Leu -15 -10 agt aay tsa gat tac agg cat gca cca cca ttc ctg gct aat ttt kgw 380 Ser Asn Xaa Asp Tyr Arg His Ala Pro Pro Phe Leu Ala Asn Phe Xaa att ttt cat aga gat gga gtt tca cca 407 Ile Phe His Arg Asp Gly Val Ser Pro 15 <210> 597 <211> 274 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 90..272 <221> sig peptide <222> 90..254 <223> Von Heijne matrix score 4 seq LHQGLCLPQRVHC/SL <400> 597 getgacegrg egeaeseege eeeeggsgee atetteeega eegegageeg teeagqtete 60 agtgetrtge ecceecaga geetagagg atg ttt cat ggg ate eca gee acg 113 Met Phe His Gly Ile Pro Ala Thr -55 ccg ggc ata gga gcc cct ggg aac aag ccg gag ctg tat gag gta cga 161 Pro Gly Ile Gly Ala Pro Gly Asn Lys Pro Glu Leu Tyr Glu Val Arg -45 -40 -35 caa cat ggc aga gct gtt tgc ggt ggt gaa gac aat gca agc cct gga 209 Gln His Gly Arg Ala Val Cys Gly Glu Asp Asn Ala Ser Pro Gly -25 -20 gaa ggc cta cat caa gga ctg tgt ctc ccc cag cga gta cac tgc agc 257 Glu Gly Leu His Gln Gly Leu Cys Leu Pro Gln Arg Val His Cys Ser -15 -10 -5 ctg ctc ccg gct cct gg 274 Leu Leu Pro Ala Pro <210> 598 <211> 417 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 343..417 <221> sig_peptide <222> 343..408 <223> Von Heijne matrix score 4 seq LFLSVLNFLFLLS/FS <400> 598 gcatctagaa gtacaagttg atgattattg tccatttgat agagacactg gaagggtgtc agtgtaaaca ctggccatgt gaagattgag cctgttgatg gtttcttttg tatcatagga 120 tgccacgtca ccaactaggg aattctgccc aatcagttga gccaaatagt gctgtcctat 180 tgtaaaattg tttaatctgt gtgcttgtgt gtgtgcttgt cagaatttgt gaatcataga 240 attgttttaa ctggaagaag acccccaaga tcatctgctt caaccccttc cttcctctc 300

321	
tttccagaga ggttgcactt tacttgagct gtgactagga tt atg cca cat tct Met Pro His Ser -20	.354
ttt gta agt tgt aac cta ttt ttg tct gtr ttg aat ttc ctt ttt ttg Phe Val Ser Cys Asn Leu Phe Leu Ser Val Leu Asn Phe Leu Phe Leu -15 -10 -5	402
cta agc ttt agc aca Leu Ser Phe Ser Thr	417
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ctc ctc agt aca ctg gct act ata gca ggc aac att tac aga Leu Leu Ser Thr Leu Ala Thr Ile Ala Gly Asn Ile Tyr Arg -10 -5 1	329
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tca gaa gca ctc ccc tcc ctt gct ggg gac cca gtg gct gtg gaa gcc Ser Glu Ala Leu Pro Ser Leu Ala Gly Asp Pro Val Ala Val Glu Ala -20 -15 -10	225
ttg ctc cgg gcc gtg ttt ggg gtt gtt gtg gat gag gcc att cag aaa Leu Leu Arg Ala Val Phe Gly Val Val Val Asp Glu Ala Ile Gln Lys	273

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-5
 gga acc agt gtc tcc cag aag gtc tgc smg tgg aag ga
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 Gly Thr Ser Val Ser Gln Lys Val Cys Xaa Trp Lys
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 gaagtgatga tgatgacaat gatgatgatg atgatgtttt agcatcagat ttccatctcc
                                                                         120
 aggaacattc taattcaaat tcatatagtt ggtccttg atg cgg ttg gcg atg gtg
                                                                         176
                                            Met Arg Leu Ala Met Val
                                                 -35
 caa ttg gtg ctc aac aat ttg aag act ttt tat ccc ttc gca gat cat
                                                                        224
 Gln Leu Val Leu Asn Asn Leu Lys Thr Phe Tyr Pro Phe Ala Asp His
                      -25
                                          -20
 gat ctt gca gag ctt cca gtt agt tca cct ctt tgt cat gcg gtt cta
                                                                        272
 Asp Leu Ala Glu Leu Pro Val Ser Ser Pro Leu Cys His Ala Val Leu
                  -10
 aaa act ctt caa tgt tgg gaa caa gtt ctt ctc cga cga ctt gaa atc
                                                                        320
 Lys Thr Leu Gln Cys Trp Glu Gln Val Leu Leu Arg Arg Leu Glu Ile
                              10
 cat ggt ggg cca cct caa aat tat atc gca agt cat acc gcc gan nag
                                                                        368
 His Gly Gly Pro Pro Gln Asn Tyr Ile Ala Ser His Thr Ala Xaa Xaa
     20
 agt ttg tct gca ggt cct gca att ctt cgc cac aaa gct tta ctg gaa
                                                                         416
 Ser Leu Ser Ala Gly Pro Ala Ile Leu Arg His Lys Ala Leu Leu Glu
 35
                                                               50 .
 cct a
                                                                         420
 Pro
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ttagggcaga gattaatgcc caccagaaag gtaactttga tgagggtagc aagcatgctt
                                                                       120
tcactgaaaa gtatttttt ttcctctttt caagattctc ataattataa cccataaaac
                                                                       180
taagttagac ttgtttctta tgtgcattta tgatttaatt aacgagagta cactttgtat
                                                                       240
gacaaaatgc aattttaagg taaacactat ggagaataat ttcttttcct agtgaa atg
                                                                       299
gtg cac gtt ata ttt tat ttt gtt tta ttt cta ggg ata atg aca cag
                                                                       347
Val His Val Ile Phe Tyr Phe Val Leu Phe Leu Gly Ile Met Thr Gln
cgg g
                                                                       351
Arg
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<222> 37..195
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                                                                       54
                                         Met His Lys Phe Phe Arg
                                         -25
cat ttc tat tca gat ttt ctg att tat ttc ttt cag ctc cat tca tgt
                                                                      102
His Phe Tyr Ser Asp Phe Leu Ile Tyr Phe Phe Gln Leu His Ser Cys
                -15
                                     -10
tgt cac gat aaa gtr act gcm cra agg gcc tat rtt cac tac agc agc
                                                                      150
Cys His Asp Lys Val Thr Ala Xaa Arg Ala Tyr Xaa His Tyr Ser Ser
ctc tta act cct tac ctc tct cag cac ccc tgc ccc cat ccc ggg
                                                                      195
Leu Leu Thr Pro Tyr Leu Ser Gln His Pro Cys Pro His Pro Gly
    15
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ca atg gcg gcc tta ggg tcc ccg tcg cac act ttt cga gga ctt ctg	107
Met Ala Ala Leu Gly Ser Pro Ser His Thr Phe Arg Gly Leu Leu	. •
-25 -20 -15	
egg gag ttg ege tac etg age geg gee ace gge cac eet ate geg aca	155
Arg Glu Leu Arg Tyr Leu Ser Ala Ala Thr Gly His Pro Ile Ala Thr	
-10 -5 1 5	
ccg cgg cct atc ggt acc ntt gtg aag gct ttc cgt gca cat cgg gtc	203
Pro Arg Pro Ile Gly Thr Xaa Val Lys Ala Phe Arg Ala His Arg Val	
10 15 20	
acc agt gaa aag ttg tgc aga gcc caa cat gag ctt cat ttc caa gct	-251
Thr Ser Glu Lys Leu Cys Arg Ala Gln His Glu Leu His Phe Gln Ala 25 30 35	
gcc acc tat ctc tgc ctc ctg cgt asa tcc gga aac atg tgg ccc tac	299
Ala Thr Tyr Leu Cys Leu Leu Arg Xaa Ser Gly Asn Met Trp Pro Tyr	. 233
40 45 50	
atc agg aat ttc atg gca agg gtg agc gct cgg tgg agg agt ctg ctg	347
Ile Arg Asn Phe Met Ala Arg Val Ser Ala Arg Trp Arg Ser Leu Leu'	511
55 60 65	
get tgg tgg gtc tca agt tgc ccc atc agc ctg gag gga agg gct ggg	395
Ala Trp Trp Val Ser Ser Cys Pro Ile Ser Leu Glu Gly Arg Ala Gly	
70 75 80 85	
agc cat gaa cat gga gaa tat cct tgg atg c	426
Ser His Glu His Gly Glu Tyr Pro Trp Met	
90 95	
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\ZZZ\/ \11100	
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actggtcagg atg atc acg gac gtg cag ctc gcc atc ttc gcc aac atg	109
Met Ile Thr Asp Val Gln Leu Ala Ile Phe Ala Asn Met	
-25 -20	
ctg ggc gtg tcg ctc ttc ttg ctt gtc gtt ctc tat cac tac gcg gcc	157
Leu Gly Val Ser Leu Phe Leu Leu Val Val Leu Tyr His Tyr Ala Ala	
-15 -10 -5 1	
gtg g	161
Val	
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tggcaggatt actatagtcc ccccaacaag ctctaccama gaagataata gaacttattg
                                                                       120
agcttaaatg aattatagga magttcctga aaagtccaar gtaaatgtga agagaacccg
                                                                       180
attetettaa eeteaceeaa eecageaett gatteteeet tgttteetgg tttteataca
                                                                       240
cacactggga aaggamaagg aagaagaaac aaggatgtcg tt atg gct gaa gga
                                                                       294
                                                Met Ala Glu Gly
get ttg age tte ett tge tet tta teg caa aat gea ttg aat att tee
                                                                       342
Ala Leu Ser Phe Leu Cys Ser Leu Ser Gln Asn Ala Leu Asn Ile Ser
                -10
ctc att tct cgt aag
                                                                       357.
Leu Ile Ser Arg Lys
<210> 609
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                                                                        60
ctgaattgaa tttagctctg tttacggttt tcttttctgt gagcagaagt tcttaatgat
                                                                       120
tactgtagtc aa atg tat cca tct ttt ctt tta tgc ttc aca ctc gta ggg
                                                                       171
              Met Tyr Pro Ser Phe Leu Leu Cys Phe Thr Leu Val Gly
                  . -15
act cag tta aga aat tct tcc tta gcc atg
                                                                       201
Thr Gln Leu Arg Asn Ser Ser Leu Ala Met
<210> 610
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<220>
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•	accgcettee cacateggat egeagggete ecaaaatgge gagtgagaet geggggaete getgageage ggaggggag egtgeagarm mgetgeggee eteacagtee ggageeegge egtgeegtge egtagggaae atgeaetttt ecatteeega aacegagtee egeagegggg acageggegg eteegeetae gtggeetata acatteaegt ga atg gag tee tge  Met Glu Ser Cys  -15	60 120 180 234
	act gtc ggg tgc gct aca gcc agc tcc tgg ggc tgy acg agc agg gg Thr Val Gly Cys Ala Thr Ala Ser Ser Trp Gly Cys Thr Ser Arg -10 -5 1	281
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	agcttccggg tttcctgggc tactacg atg gcg atg agt ttc gag tgg ccg tgg  Met Ala Met Ser Phe Glu Trp Pro Trp  -40  -35	54
	cag tat cgc ttc cca ccc ttc ttt acg tta caa ccg aat gtg gac act Gln Tyr Arg Phe Pro Pro Phe Phe Thr Leu Gln Pro Asn Val Asp Thr -30 -25	102
	-30 -25 -20  cgg cag aag cag ctg gcc gcc tgg tgc tcg ctg gtc ctg tcc ttc tgc  Arg Gln Lys Gln Leu Ala Ala Trp Cys Ser Leu Val Leu Ser Phe Cys -15 -10 -5	150
	cgc ctg cac aaa cag tcc agc atg acg gtg atg gaa gct cag gag agc Arg Leu His Lys Gln Ser Ser Met Thr Val Met Glu Ala Gln Glu Ser	198
	ccg ctc ttc aac aac gtc aag cta cag cga aag ctt cct gtg g Pro Leu Phe Asn Asn Val Lys Leu Gln Arg Lys Leu Pro Val 15 20 25	241
. •	<210> 612 <211> 176 <212> DNA <213> Homo sapiens	
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	<400> 612 aagagcettg gaacatetet etgaagaata aaacaaatet tttetgeatg tataategat ataaatttga ttatattgta etttttattt egtgtgtgtg tgtae atg aga tta eat	60 117
	Met Arg Leu His gta cat tcc ctt tct ccc ttt tcc ttt gct tgt ctc cct ttt ctg tcc Val His Ser Leu Ser Pro Phe Ser Phe Ala Cys Leu Pro Phe Leu Ser	165

WO 99/53051 PCT/IB99/00712 328 -10 -5 1 ccc ccg ctg gg 176 Pro Pro Leu <210> 613 <211> 342 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 258..341 <221> sig_peptide <222> 258..335 <223> Von Heijne matrix score 3.90000009536743 seq RMCILQLLSAVLY/RF <400> 613 catttctatk aaaatacaaa tttaaggctg tagatttaat atgtagtatg ttcattrrqt. 60 tccaaataca ttctaatttc cactgtgatt tctwctttga ctcmtgaawt atttaqvaqq 120 tgwttttgwh ttabdwattt ctgactgtat ggggattttc tagttagttt wctactctta 180 attigictic agagamaata ciccacaaga titcagicti tcaattitigi igcaactiqc 240 tacaaacttg gcctaac atg ttg cat ttt wta tat atg atc caw gtg tgc 290 Met Leu His Phe Xaa Tyr Met Ile Xaa Val Cys -25 -20 ttg gaa aga atg tgc att ctg caa ttg ttg agt gct gtg ttg tat aga 338 Leu Glu Arg Met Cys Ile Leu Gln Leu Leu Ser Ala Val Leu Tyr Arg -15 -10 -5 ttt g 342 Phe <210> 614 <211> 154 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 48..152 <221> sig_peptide <222> 48..137 <223> Von Heijne matrix score 3.90000009536743 seq VGLLDTPLGAVSA/HH <221> misc feature <222> 17 <223> n=a, g, c or t <400> 614 agtoggagog aaggvontgg oggasagaac ggattgcagg gtoagco atg toa tot -30 gag cet ecc eca eca eca cag ecc ecc acc eat eaa get tea gte ggg 104 Glu Pro Pro Pro Pro Gln Pro Pro Thr His Gln Ala Ser Val Gly -20 etg etg gac acc ecc etc gga gec gtg age get eac eat ecc etc tge 152

Leu Leu Asp Thr Pro Leu Gly Ala Val Ser Ala His His Pro Leu Cys

-5

-10

CC

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                                                                       60
ttatctttga caaaataatt tctctgatgc ctgactgcct gcccccaac aacaaagctt
                                                                      120
ttattatact tcttaactaa tcaactatwm cyttacccat ctagccaaag tagactaccc
                                                                      180
atat atg ttt ctt gac cat gtc agg ttt tta acc tcc ata tct ttt ctt
                                                                      229
     Met Phe Leu Asp His Val Arg Phe Leu Thr Ser Ile Ser Phe Leu
                         -15
                                              -10
gct ctg gtc ctg tgg aat gtc ttt ctc aac tct acc cgt ctg g
                                                                      272
Ala Leu Val Leu Trp Asn Val Phe Leu Asn Ser Thr Arg Leu
-5
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                                                                       53
                                       Met Arg Glu Lys Pro Gln
                                                        -15
cca gcg ctc ctg act tca agt gar ctg cct gcc ttg gcc tct caa ata
                                                                      101
Pro Ala Leu Leu Thr Ser Ser Glu Leu Pro Ala Leu Ala Ser Gln Ile
            -10
                                -5
cat tgc cgc gtc c
                                                                      114
His Cys Arg Val
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                                                                        58
ccc cac aac cac ttg gag gga gat gct ttg ctg aga gtc cct gtc ctc
                                                                       106
Pro His Asn His Leu Glu Gly Asp Ala Leu Leu Arg Val Pro Val Leu
                    -20
                                         -15
tgc atc tgg aga gct tgg ctc aga gct gag gtg gga ggg agg gct cct
                                                                       154
Cys Ile Trp Arg Ala Trp Leu Arg Ala Glu Val Gly Gly Arg Ala Pro
                - 5
                                    1
ctt cca ggt cgc atg gg
                                                                       171
Leu Pro Gly Arg Met
        10
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                                                                      120
ctgtgaaata ctttaaatat gagttgttgg gaaagttaa atg aaa aat act ctt
                                                                      174
                                           Met Lys Asn Thr Leu
                                                    -20
tat tat aat ttt tgt tta ttt tgg att ytc cta cct ccc cac aca tgc
                                                                      222
Tyr Tyr Asn Phe Cys Leu Phe Trp Ile Xaa Leu Pro Pro His Thr Cys
        -15
aca cac aca gac aca cat
                                                                      240
Thr His Thr Asp Thr His
   1
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geactettte etetgeatee cetteeetge ggeece atg tge etg aac eee gee
                                                                       114
                                         Met Cys Leu Asn Pro Ala
tgc tcg gga ccg ctt tcc ctc cgt tcc cct cgg ctt ccc cct ctc ttt
                                                                       162
Cys Ser Gly Pro Leu Ser Leu Arg Ser Pro Arg Leu Pro Pro Leu Phe
                ~25
                                     -20
tgc act ttt ctt tcc ctt tct ttg cat ccc tgg ggg ggt ttc ttt ttg
                                                                       210
Cys Thr Phe Leu Ser Leu Ser Leu His Pro Trp Gly Gly Phe Phe Leu
                                 -5
tgt gcc tgg att tct bkt ttc ctc ccg tgg gtg tgt gtg tgk gcg gg
                                                                      257
Cys Ala Trp Ile Ser Xaa Phe Leu Pro Trp Val Cys Val Xaa Ala
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                                                                       55
                                                    Met Ala His
tca aag act agg acc aat gat gga aaa att aca tat ccg cct ggg gtc
                                                                      103
Ser Lys Thr Arg Thr Asn Asp Gly Lys Ile Thr Tyr Pro Pro Gly Val
                        -80
aag gaa ata tca gat aaa ata tct aaa gag gag atg gtg aga cga tta
                                                                      151
Lys Glu Ile Ser Asp Lys Ile Ser Lys Glu Glu Met Val Arg Arg Leu
                    -65
                                        -60
aag atg gtt gtg aaa act ttt atg gat atg gac cag gac tct gaa gaa
                                                                      199
Lys Met Val Val Lys Thr Phe Met Asp Met Asp Gln Asp Ser Glu Glu
                -50
                                    -45
                                 .
gaa aag gag ctt tat tta aac cta gct tta cat ctt gct tca gat ttt
                                                                      247
Glu Lys Glu Leu Tyr Leu Asn Leu Ala Leu His Leu Ala Ser Asp Phe
                                -30
ttt ctc aag cat cct gat aaa gat gtt cgc tta ctg gta gcc tgc tgc
                                                                      295
Phe Leu Lys His Pro Asp Lys Asp Val Arg Leu Leu Val Ala Cys Cys
        -20
                            -15
ctt gct gat att ttc agg att tat gct cct gaa gct cct tac aca tcc
                                                                      343
Leu Ala Asp Ile Phe Arg Ile Tyr Ala Pro Glu Ala Pro Tyr Thr Ser
                                                             10
cct aag gg
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Pro Lys
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ttttttaaaa aattcacttg tttttctcga gaatttgtga ctgatttta tgttatactg	240
cataattcag taatttcaca cattaacaac atccagggtc atgtgaggat gagttttcta	300
gcttctgaaa tgttctgagg atgtaatttt ttaataagag gaa atg tnn tct cac	355
Met Xaa Ser His	
-25	400
aga cta ttt ggg tgt ttt cca agt gac ttg tca cga atg gtt ttg ctc Arg Leu Phe Gly Cys Phe Pro Ser Asp Leu Ser Arg Met Val Leu Leu	403
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Ser Ser Ala Leu Leu Ser Thr Glu Asn	
-5 1	
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ggt Gly	999 Gly	cgc Arg 1	cag Gln	ggc Gly	ttc Phe	acc Thr 5	tcc Ser	aag Lys	gcg Ala	gat Asp	cct Pro 10	cag Gln	ggc	agt	ggc , Gly	99
Arg 15	Ile	Thr	gct Ala	Ala	Val 20	Ile	Glu	His	Leu	Glu 25	cgt Arg	Leu	Ala	Leu	Val 30	147
Asp	Phe	Gly	agc Ser	Arg 35	Glu	Ala	Val	Ala	Arg 40	Leu	Glu	Lys	Ala	Ile 45	Ala	195
ttc Phe	gcc Ala	gac Asp	cgg Arg 50	cta Leu	cgc Arg	gcc Ala	gtg Val	gac Asp 55	aca Thr	gac Asp	Gly	gtg Val	gag Glu 60	ccc Pro	atg Met	243
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ccc Pro	ggc Gly	gaa Glu -70	cgt Arg	ctg Leu	tgt Cys	aac Asn	ttg Leu -65	gag	gag	ggc Gly	agc Ser	ccg Pro -60	ggc	agc	ggc Gly	101
			cgc Arg													149
			agc Ser													197
gaa Glu	aca Thr	gag Glu	tcc Ser	cag Gln -20	tta Leu	ctg Leu	cca Pro	gat Asp	gtg Val -15	gga Gly	gct Ala	att Ile	gta Val	acc Thr -10	tgt	245
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                                                                       120
gccaccattt gggcagcccc agcccatcta cccagggtat catcagtcca gct atg
                                                                       176
gtg ggc aat cag ggt cca cag ccc ccg cca ttc cct atg gag cct aca
                                                                       224
Val Gly Asn Gln Gly Pro Gln Pro Pro Pro Phe Pro Met Glu Pro Thr
                -55
                                     -50
atg gcc cag tac cag gct atc agc aaa cac ctc ccc aag gta tgt caa
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Met Ala Gln Tyr Gln Ala Ile Ser Lys His Leu Pro Lys Val Cys Gln
                                 -35
gag ccc cac ctt cct cgg ggg cac ctc cag cct caa caq cac aqq ctc
                                                                       320
Glu Pro His Leu Pro Arg Gly His Leu Gln Pro Gln Gln His Arg Leu
        -25
                            -20
ett gtg gcc agg ctg cat atg gcc agt ttg gca agg aga tgt aca gaa
                                                                       368
Leu Val Ala Arg Leu His Met Ala Ser Leu Ala Arg Arg Cys Thr Glu
    -10
                        -5
tgg gcc aag ctc cac tgt tca gat gca agg ctg ccc tgg gtc tca gc
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gtg agt gtt aca gtt ctt aaa gat ggt gtg gct gga gtt tgt ttc ttc Val Ser Val Thr Val Leu Lys Asp Gly Val Ala Gly Val Cys Phe Phe -20 -15 -10	282
aga cgt tca gat gcg tct gaa gtt tct tcc ttc tgg Arg Arg Ser Asp Ala Ser Glu Val Ser Ser Phe Trp -5 5	318
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tgt atg cct tct ttt gaa aag tgt ctg ttc tta tct ttt gcc cac ttc Cys Met Pro Ser Phe Glu Lys Cys Leu Phe Leu Ser Phe Ala His Phe -15 -10 -5	148
ttg atg gga aga acc cac cgt g Leu Met Gly Arg Thr His Arg 1	170
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agt ctc tta tca gat ata tta ttt gca aat att ttc tcc cat tct tgg Ser Leu Leu Ser Asp Ile Leu Phe Ala Asn Ile Phe Ser His Ser Trp	161

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tggataaacc atacctctag attccttgct tccattttcc cagaaacaag atg agg  Met Arg	176
aag aga aag atc agt gtg tgt caa caa act tgg gcc tta tta tgc aag	224
Lys Arg Lys Ile Ser Val Cys Gln Gln Thr Trp Ala Leu Leu Cys Lys -45 -40 -35	224
aac ttt ctt aaa aaa tgg aga atg aaa aga gag tcc tta atg gaa tgg	272
Asn Phe Leu Lys Lys Trp Arg Met Lys Arg Glu Ser Leu Met Glu Trp	
-30 -25 -20 -15	
ctg aat toa ttg ctc cta cta ctt tgt ttg tat ata tat cct cat agt	320
Leu Asn Ser Leu Leu Leu Leu Cys Leu Tyr Ile Tyr Pro His Ser -10 -5 1	
cat caa gta aat gaw tdd tct tca ctg ctt acc atg gac ctg gga cgg	368
His Gln Val Asn Xaa Xaa Ser Ser Leu Leu Thr Met Asp Leu Gly Arg 5 10 15	
gta gat rnn tkt aat gaa too aga ttt tot gtt gta tac aca cot gto	416
Val Asp Xaa Xaa Asn Glu Ser Arg Phe Ser Val Val Tyr Thr Pro Val 20 25 30	
acc aac acg acc cct gg	433
Thr Asn Thr Pro	133
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ccc aga cag Pro Arg Gln		_					. 103
aag agc aca Lys Ser Thr 1						_	151
att acc aga Ile Thr Arg 15	Lys Gly					•	172
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mag ctt gct Xaa Leu Ala						g His Pro	162
tac ctg acc Tyr Leu Thr -20							210
ccg tcc cca Pro Ser Pro							253
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                                   Met Cys Pro Ala Trp Leu Pro
tgt tgg acg gca cag acg gaa cat ctc gat cgt tac agg aag ttc cac
                                                                       100
Cys Trp Thr Ala Gln Thr Glu His Leu Asp Arg Tyr Arg Lys Phe His
        -25
                            -20
cag atg gcg ctg tyt cca ggg aca tct agg gca cag gcc tta ctt tat
                                                                      148
Gln Met Ala Leu Xaa Pro Gly Thr Ser Arg Ala Gln Ala Leu Leu Tyr
                        -5
aac gaa gtc cta gag aga ttt atg ttc acc cgg ctg c
                                                                      185
Asn Glu Val Leu Glu Arg Phe Met Phe Thr Arg Leu
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              Met Asn Val Met Lys Arg Ile Cys Thr Phe Leu Leu Pro
tca cac tct acc tct ggc cct ctg tgc tgt tca aat gcc cat ctt cct
                                                                      159
Ser His Ser Thr Ser Gly Pro Leu Cys Cys Ser Asn Ala His Leu Pro
-5
                    1
gct acc tcc tct acc ttg aaa cat tgc agg gct tgg agg gaa gcg bv
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Ala Thr Ser Ser Thr Leu Lys His Cys Arg Ala Trp Arg Glu Ala
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taagagetga gegeastgae aactagggge eggaeegteg eaggaggegt eegetggata cetteccect tecetgacet agagetetae agetgetgee teggtactga cegagggtte 240 ccagagetgt ctyaccattg caaaaacgtt atagcaacag cetetgatta egac atg 297 get gag atc acc aat atc ega cet age ttt gat gtg tea eeg gtg gtg 345 Ala Glu Ile Thr Asn Ile Arg Pro Ser Phe Asp Val Ser Pro Val Val -35 -30 gec ggc ctc atc ggg gcc tct gtg ctg gtg gtg tgt gtc tcg gtg acc 393 Ala Gly Leu Ile Gly Ala Ser Val Leu Val Val Cys Val Ser Val Thr -20 -15 -10 gtc ttt gtc tgg tca tgc tgc crc cag cag gca gag aag aag cac aag 441 Val Phe Val Trp Ser Cys Cys Xaa Gln Gln Ala Glu Lys Lys His Lys aac cca cca tac aag ttt att cac atg ctc aaa ggc wtc agc 483 Asn Pro Pro Tyr Lys Phe Ile His Met Leu Lys Gly Xaa Ser 15 <210> 642 <211> 309 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 235..309 <221> sig_peptide <222> 235..279 <223> Von Heijne matrix score 3.79999995231628 seq ILTMLILLIHEHG/IF <400> 642 attratctat gtgtctgttg ttatacgaat atcatgctgt tttggtttct atatccttgt 60 aatatgtttt gaagtcaggt agtgtgatgc ctccagattt gttctttttg gtcaggattg 120 ctttggctgw tttgggttcw wttwtggttc catacaaatt ttaggattat tttttctatg 180 totgtgaaaa gtggcatggg tattacattc aatotgtaga ttgctttgga tagt atg 237 gtc att tta act atg tta att ctt tta atc cat gag cat ggt att ttc 285 Val Ile Leu Thr Met Leu Ile Leu Leu Ile His Glu His Gly Ile Phe -10 ttt tca ctt gtt tgt gtc ctc ttc 309 Phe Ser Leu Val Cys Val Leu Phe <210> 643 <211> 245 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 147..245 <221> sig_peptide <222> 147..233 <223> Von Heijne matrix score 3.79999995231628 seq LTHTHTCTPPSTA/HP <221> misc_feature

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	12
	17:
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-25	
•	22:
yr Thr Pro Gln His Ser Pro Leu Thr His Thr His Thr Cys Thr Pro	
20 -15 -10 -5	
	24!
ro Ser Thr Ala His Pro Arg Gly	
1	
210> 644	
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213> Homo sapiens	
•	
220>	
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score 3.79999995231628	
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400 (44	
400> 644	٠,
	60
	L20 L73
gcgtgcgtg cacgcgcctg tgt atg ttt kat atg att tta ctt tgt ttt ttg 1  Met Phe Xaa Met Ile Leu Leu Cys Phe Leu	. / -
-15 -10	
=-	21:
la Val Ser Asn Phe Asn Lys Leu Leu Trp Gly Xaa	
5 1 5	
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212> DNA	
213> Homo sapiens	
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221> CDS	
222> 698	
221> sig_peptide	
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seq LPLACFSLFGXLP/QG	
400> 645	٠
	5(
Met Phe Leu Ile Leu Gly Lys Phe Ser Arg Val Met Gly Leu Pro	
-25 -20 -15	
3 333	98
eu Ala Cys Phe Ser Leu Phe Gly Xaa Leu Pro Gln Gly Leu Leu Ile	

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                                                                       120
gaatttaata gggaagaaag agacagtata actcaccagt gctgggtctc atcatcctgc
                                                                       180
aatttcdgaa caactatgaa tacaaaaaga attttaaaaat cccagtcctg cctagaaagg
                                                                       240
ggaagtcatc tctaaat atg gtg gcc ctg ggg cag ctg gcc tdc ctg cca
                                                                       290
                   Met Val Ala Leu Gly Gln Leu Ala Xaa Leu Pro
                                   -15
gge nbc tdc cat ggg ggc ctt tct gca gtg act gtg gtt ctt ccc att
                                                                       338
Gly Xaa Xaa His Gly Gly Leu Ser Ala Val Thr Val Val Leu Pro Ile
                                                                       347
tta ctc tgt
Leu Leu Cys
    10
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                                                                       110
                  Met Pro Val Ser Phe Val Cys Leu Leu Phe Arg
                   -15
aat gtt tat tca aat cta ttg cct tct ttt ttt
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Asn Val Tyr Ser Asn Leu Leu Pro Ser Phe Phe
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Met Gly Ser Gly Gly

-25

gac agc ctc ctg ggg ggc agg ggt tcc ctg cct ctg ctc cct gct 103
Asp Ser Leu Leu Gly Gly Arg Gly Ser Leu Pro Leu Leu Pro Ala
-20 -15 -10

cat cat ggg agg cat ggc tca gga ctc ccc gcc cca gat cct agt cca 151
His His Gly Arg His Gly Ser Gly Leu Pro Ala Pro Asp Pro Ser Pro
-5 1 5 10

ccc cca gga cca gct gtt cca ggg ccc tgg ccc tgc cag gat gag ctg
Pro Pro Gly Pro Ala Val Pro Gly Pro Trp Pro Cys Gln Asp Glu Leu

15 20 25

cca agc ctc agg cca gcc acc tcc cac cac ttt

Pro Ser Leu Arg Pro Ala Thr Ser His His Phe

30

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-25

-15

aga tct gga ttc tcg ttt cag gtt tcg ggg tgg ggg tgg gga gaa agg 96
Arg Ser Gly Phe Ser Phe Gln Val Ser Gly Trp Gly Trp Gly Glu Arg
-10 -5

gtc gat gat ttc ctt ttt tcg tcg ggt ata gac ggr a 133
Val Asp Asp Phe Leu Phe Ser Ser Gly Ile Asp Gly

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ctt Leu	gct Ala	cac	cac His	cca	aga	20 acc	: tca	gga	cag	- aag	15 cga	gaq	ccc	att Ile	-10	
	_	_		agc Ser	_	_			1			•	5		•	419
<21 <21	0 > 6 1 > 3 2 > D 3 > H	96 NA	sapi	ens				-			•					
	0> 1> C 2> 5		96													
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	0> 6! gaagi		tgtg	gaga	cg g	agga	cagg	a gc	agtg	ccca	agc	agcga	agg ·		g ctg t <b>Le</b> u	57
atc Ile	ttg Leu -70	aat Asn	ggc Gly	ttc Phe	cgg Arg	ggc Gly -65	cat His	gcc Ala	aca Thr	gat Asp	tcc Ser -60	gtg Val	aag Lys	aac Asn	tcc	105
Met -55	Glu	Ser	Met	Asn	Thr -50	Asp	Met	Val	Ile	Ile -45	Pro	Gly	Gly	ctg Leu	Thr	153
Ser	Gln	Leu	Gln	Val -35	Leu	Asp	Val	Val	Val -30	Tyr	Lys	Pro	Leu	aat Asn -25	Asp	201
Ser	Val	Arg	Ala -20	Gln	Tyr	Ser	Asn	Trp -15	Leu	Leu	Ala	Gly	Asn -10	ctg Leu	Ala	249
Leu	Ser	Pro -5	Thr	Gly	Asn	Ala	Lys 1	Lys	Pro	Pro	Leu 5	Gly	Leu	ttt Phe	Leu	297
Glu 10	Trp	Val	Met	Val	Ala 15	Trp	Asn	Ser	Ile	Ser 20	Ser	Glu	Ser	atc Ile	Val 25	345
caa Gln	999 Gly	whc Xaa	aaa Lys	gaa Glu 30	gtg Val	cca Pro	tat Tyr	ctc Leu	crg Xaa 35	caa Gln	ctt Leu	gga Gly	gga Gly	gga Gly 40	aga Arg	393
cga																396

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                                                                       108
       Met Ile Cys Thr Thr Val Tyr Ile Thr Met Ala Pro Tyr Cys
                           -20
cta tca aac tgt tta ctt thw caw agt tgg ggc ctg cat ttg tat aga
                                                                       156
Leu Ser Asn Cys Leu Leu Xaa Xaa Ser Trp Gly Leu His Leu Tyr Arg
ttt cta gcc ccc at
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Phe Leu Ala Pro
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ctctgggaac aggaaagtca ggaaccctgc ctttcaggaa ctgctgtatc tcagtcggct
                                                                       120
tetteattte atg gtt tet ete tgt gta get get tta ttt eet ett eag
                                                                       169
           Met Val Ser Leu Cys Val Ala Ala Leu Phe Pro Leu Gln
                           -10
                                                                     . 178
gct tac ggg
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atacaatgtt tggttttcca ttcctgagtt acttcactta gaataatagt ctccaatctc
                                                                   120
atccaggtca ctgcaa atg cca ttg gtt cat tcc ttc tta tgg ctg agt agt
                                                                   172
                 Met Pro Leu Val His Ser Phe Leu Trp Leu Ser Ser
                  -15
atc cta tat ata tac cac ctg cgg g
                                                                   197
Ile Leu Tyr Ile Tyr His Leu Arg
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111
                   Met Ile Ser Asn Gly Lys Phe Phe Cys Phe Phe
                                   -20
ttk gtt ttt kgt ttt tkg ttt ttg ara cgg asy ttg cyc tkg ycg ccc
                                                                   159
Xaa Val Phe Xaa Phe Xaa Phe Leu Xaa Arg Xaa Leu Xaa Xaa Pro
           -10
agg ctg gag tgc aat ggm aar ayc tcg gcy cac tgm aac ctc cgc ctc
                                                                   207
Arg Leu Glu Cys Asn Gly Lys Xaa Ser Ala His Xaa Asn Leu Arg Leu
ctg agt yea age aat tey etk gee tea gee eec ega ggg
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Leu Ser Xaa Ser Asn Ser Leu Ala Ser Ala Pro Arg Gly
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Phe Ser Leu Glu Glu Trp Ser Leu 15

<210> 661

<211> 411

<212> DNA

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1 5 10 ggv caa caa wat cac tgt aac ta

ggv caa caa wat cac tgt aac ta

Gly Gln Gln Xaa His Cys Asn

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<210> 662

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353

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                                         Met Ser Leu Pro Pro Phe
                                          -30
tte cae cet tet cee get cee tet ete get cee cet cee tee ete ttt
                                                                      103
Phe His Pro Ser Pro Ala Pro Ser Leu Ala Pro Pro Pro Ser Leu Phe
                -20
                                 -15
                                                         -10
ctt tcc ctc cct ccc tct ctt tct ccc cct cta ccc gcc cgg g
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Leu Ser Leu Pro Pro Ser Leu Ser Pro Pro Leu Pro Ala Arg
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                      -10
ttt ttt ttt ttt tt
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Phe Phe Phe Phe
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cgggatgccg gagccctcgg gccttggag		Gly Pro Cys Ser	
cag gag gga ggg agg cag tgg gct Gln Glu Gly Gly Arg Gln Trp Ala -30	cat ggg tcg	gtg cct ttg cag	ccg 101
aca gca cgc ctt gcg gcc ctg ggg Thr Ala Arg Leu Ala Ala Leu Gly -15			
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attittaca gaaagtotgg ctattgccta			
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ttt cag aaa aac aaa acc aac ctg t Phe Gln Lys Asn Lys Thr Asn Leu 1 -15			
cag agt tac aat tgg ctg aat att t Gln Ser Tyr Asn Trp Leu Asn Ile 1 1 5			
ctc ttc att tca gta att aam aca a Leu Phe Ile Ser Val Ile Xaa Thr a	Asn Phe Leu	Lys Arg Tyr Leu I	eu .
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tttgactgtg gcaagtaaag atgctatgaa cattcatgta cacatgaatt tgtaqqcat atg ttt tta ttt tgc tgg gag aaa agc cca aga atg cag ttg ctg ggt Met Phe Leu Phe Cys Trp Glu Lys Ser Pro Arg Met Gln Leu Leu Gly -20 -15 tgt atg gta ttg tat gat tgt ttt tct ttt aag aaa ctg ccg ggg g 273 Cys Met Val Leu Tyr Asp Cys Phe Ser Phe Lys Lys Leu Pro Gly <210> 667 <211> 149 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 8..148 <221> sig_peptide <222> 8..97 <223> Von Heijne matrix score 3.7000004768372 seq FVCFFHVFYCVFC/NV <400> 667 attitgt atg tot tit ata tot git att tit cot tia atc cit tia aac 49 Met Ser Phe Ile Ser Val Ile Phe Pro Leu Ile Leu Leu Asn -25 -20 cgt ttt tca ttt gtt tgt ttc ttt cat gtc ttt tac tgt gtt ttc tgc 97 Arg Phe Ser Phe Val Cys Phe Phe His Val Phe Tyr Cys Val Phe Cys -10 aac gtc tct tct ttg ttc tcc tat cag ttt ctt ctt cat ttc tgt gat 145 Asn Val Ser Ser Leu Phe Ser Tyr Gln Phe Leu Leu His Phe Cys Asp gac t 149 Asp <210> 668 <211> 122 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 16..120 <221> sig_peptide <222> 16..108 <223> Von Heijne matrix score 3.70000004768372 seq LGMGMGFFSGVKS/WI <400> 668 caaggaatta cagaa atg cat gaa tac tta cct aga aac ttt cat gac ttt 51

356

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                                                                       - 55
                                          Met Ala Ser Xaa Val Pro
                                              -35
qtq aaq qac aag aaa ctt ctg gag gtc aaa ctg ggg gag ctg cca agc .
                                                                       103
Val Lys Asp Lys Lys Leu Leu Glu Val Lys Leu Gly Glu Leu Pro Ser
                    -25
                                         -20
tgg atc ttg atg cgg gac ttc agt cct agt ggc att ttc gga gcg ttt
                                                                       151
Trp Ile Leu Met Arg Asp Phe Ser Pro Ser Gly Ile Phe Gly Ala Phe
                -10
                                     -5
caa aga ggt tac tac cgg tac tac aac aag tac atc aat gtg aag aag
                                                                       199
Gln Arg Gly Tyr Tyr Arg Tyr Tyr Asn Lys Tyr Ile Asn Val Lys Lys
                            10
qqq aqc atc tcg ggg att acc atg gtg ctg gca tgc tac gtg ctc ttt
                                                                       247
Gly Ser Ile Ser Gly Ile Thr Met Val Leu Ala Cys Tyr Val Leu Phe
                        25
                                             30
                                                                       288
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                                                                       112
                               Met Val Ile Ser Ala Gly Ala Leu
                                            -15
ctg tgg atg gcg tgg gac ggc cag ctc agc cgc ccc gaa ggc gcc cgt
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aat c Asn L	Leu	Glu	Leu	Leu -10	Gly	Ser	Ser	Tyr	Asn -5	Pro	Ile	tca Ser	gcc Ala	tct Ser 1	cca Pro		103
gta g Val A	Ala	agg Arg 5	act Thr	ata Ile	tca Ser	tgc Cys	ccc Pro 10	gct Ala	att Ile	gtg Val	g						137
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ggc (	tct Ser -85	gga Gly	ttt Phe	aaa Lys	gct Ala	gag Glu -80	cgc Arg	tta Leu	aga Arg	gtg Val	aat Asn -75	ttg Leu	aga Arg	tta Leu	gtc Val		164
ata i Ile i -70	Asn	Arg	Leu	Lys	Leu -65	Leu	Glu	Lys	Lys	-60	Thr	Glu	Leu	Ala	Gln -55		212
aaa ( Lys .	Ala	Arg	Lys	Glu -50	Ile	Ala	Asp	Tyr	Leu -45	Ala	Ala	Gly	Lys	Asp -40	Glu		260
cga Arg	Ala	Arg	11e -35	Arg	Val	Glu	His	11e -30	Ile	Arg	Glu	Asp	Tyr -25	Leu	Val		308
gag Glu	Ala	Met -20	Glu	Ile	Leu	Glu	Leu -15	Tyr	Cys	Asp	Leu	Leu -10	Leu	Ala	Arg		356
Phe	Gly -5	Leu	Ile	Gln	Ser	Met 1	Lys	Glu	Leu	Asp .5	Ser	Gly	Leu	Ala	gaa Glu 10		404
Ser	Val	Ser	Thr	Leu 15	Ile	Trp	Ala	Ala	Pro 20	Arg	Leu	Gln	Ser	gaa Glu 25	gtg Val		452
gct Ala	gag Glu	ttg Leu	aaa Lys	ata Ile	gtt Val	gct	gat Asp	cag Gln	ctc Leu	tgt Cys	cca Pro	agt Ser	at				493

213

30

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att tgc ttt ttt cgc tta aca atc tta gkt ttc cat gac aat aca tgg

Ile Cys Phe Phe Arg Leu Thr Ile Leu Xaa Phe His Asp Asn Thr Trp

359 -15 -10 ggg tca act tca ttc tct twa gtt gck gca atg cta ttc cac tac cgg 261 Gly Ser Thr Ser Phe Ser Xaa Val Ala Ala Met Leu Phe His Tyr Arg gg · 263 <210> 675 <211> 107 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 30..107 <221> sig_peptide <222> 30..101 <223> Von Heijne matrix score 3.70000004768372 seq LLFLFFLFFFFF/FF <400> 675 tgcactggca cacactcaca gctctgacc atg tca tca aac ata cag aga ctg 53 Met Ser Ser Asn Ile Gln Arg Leu -20 ggc ttc cct ctg ctt ttt ctt ttt ctt ttt ctt ttt ctt ttt ttt ttt 101 Gly Phe Pro Leu Leu Phe Leu Phe Phe Leu Phe Leu Phe Phe Phe -15 -10 ttt ttt 107 Phe Phe <210> 676 <211> 276 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 70..276 <221> sig_peptide <222> 70..270 <223> Von Heijne matrix score 3.70000004768372 seq LVLPLPMLPTSNR/KR <400> 676 gtcacagcac cctcctgaaa actgcagctt ccttctcacc ttgaagaata atcctagaaa 60 acticacaaa atg tgt gat gct ttt gta ggt acc tgg aaa ctt gtc tcc agt 111 Met Cys Asp Ala Phe Val Gly Thr Trp Lys Leu Val Ser Ser -65 gaa aac ttt gat gat tat atg aaa gaa gta gga gtg ggc ttt gcc acc 159 Glu Asn Phe Asp Asp Tyr Met Lys Glu Val Gly Val Gly Phe Ala Thr -45 agg aaa gtg gct ggc atg gcc aaa cct aac atg atc atc agt gtg aat 207 Arg Lys Val Ala Gly Met Ala Lys Pro Asn Met Ile Ile Ser Val Asn -35 -30 -25 ggg gat gtg atc acc att ccc cac ctg gtc ctc ccc ctt ccc atg ctg 255 Gly Asp Val Ile Thr Ile Pro His Leu Val Leu Pro Leu Pro Met Leu -10 276 cca act tct aac cgc aag agg Pro Thr Ser Asn Arg Lys Arg

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360
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                                                                       120
agggttggac acgatggaaa tattttggtg aaccattcgt tcccttgggt ttctttctca
                                                                       180
tttggggagt gtggtttaca atgattggag caaaagtttc ctgaatcttt ttcttgtttc
                                                                       240
cattttattg catggtaaaa cacaatttat ccactttctt gtcaatgagt atctagttag
                                                                       300
attcctgttt tttggctaat tcaaataaaa ctatga atg ttt ttg tac cgg tct
                                                                       354
                                         Met Phe Leu Tyr Arg Ser
                                              -20
ttt ggt ggg cag ttg ctt tcc ttt ctc ttg ggt aca tac cta gga agg
                                                                       402
Phe Gly Gln Leu Leu Ser Phe Leu Leu Gly Thr Tyr Leu Gly Arg
                    -10
                                         -5
agg gaa gtt gct ggg cca cag cat ggc cag ttt tct aaa
                                                                       441
Arg Glu Val Ala Gly Pro Gln His Gly Gln Phe Ser Lys
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gactggcttc gggagaaaca ccatccagaa gagacctttc aaaaaacttc tagagactcc
                                                                       120
ccaagacgta tgag atg ama ggc ttc ttc tgt ctg tgt gcg ttt aac tca
                                                                       170
                Met Xaa Gly Phe Phe Cys Leu Cys Ala Phe Asn Ser
ttt ctc ctt agc ccc gag ggg
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Phe Leu Leu Ser Pro Glu Gly
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-10

370

gtg act cat cca aac tcc atg cca gct gtc aac att cag tat gaa gtc

Val Thr His Pro Asn Ser Met Pro Ala Val Asn Ile Gln Tyr Glu Val

score 3.59999990463257 seq STFALTIXRXXSC/SS <221> misc_feature <222> 102 <223> n=a, g, c or t

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55

303

Thr Arg Ser Thr Gln Gln Leu Phe Ala Gln Ser Trp Ser Leu Ser Xaa

50

<210> 682 <211> 328 <212> DNA <213> Homo sapiens

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<220>

aag atg atg c

Lys Met Met

<221> misc_feature

<222> 258 <223> n=a, g, c or t

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	60
acccaatgaa agaagaaa atg aaa gcc ata aag aaa agt ctt aca gaa gaa 11 Met Lys Ala Ile Lys Lys Ser Leu Thr Glu Glu -40 -35	11
gaa tac ctg tac ctg gac ttt tct cac caa aca gaa gga tgc atc ttt Glu Tyr Leu Tyr Leu Asp Phe Ser His Gln Thr Glu Gly Cys Ile Phe	59
-30 -25 -20 -15  cct ctt cat aca tct gta act tta ttt ctg tta tct tac tgt gac tgt 20  Pro Leu His Thr Ser Val Thr Leu Phe Leu Leu Ser Tyr Cys Asp Cys	<b>)</b> 7
-10 -5 1  aaa atc ttt aaa att tgc tta gtt gtc acc aaa gag gtg agt aga gat 25	55
Lys Ile Phe Lys Ile Cys Leu Val Val Thr Lys Glu Val Ser Arg Asp 5 10 15	-
avn tca cta cta aga gat gac ctg atc cag gat gtt gaa ata cag att Xaa Ser Leu Leu Arg Asp Asp Leu Ile Gln Asp Val Glu Ile Gln Ile 20 25 30	)3
20 25 30 att tca agg cag gag ctc cca cca a 32 Ile Ser Arg Gln Glu Leu Pro Pro	28
35 40	
<210> 683 <211> 447 <212> DNA	٠
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score 3.59999990463257 seq FLCVCYFIRKSTS/FF	
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taaggtatag gaaggtattt aagaaagaag caaacattct ctagatgttg ttatccaaaa 12 tatattctct tttgcagttt actgaaataa tttcttcagt gtgtgggaat ttcctttgca 18	30
tccagcttta ctatagagat gacatcacac caacagtgac acgacttgtt tacaagaggg 24 tggtataaac agcaaatgtt cttccttaaa acagatttct tgttgaactt caacagaaaa 30 agaagcngta aatgtagaag gaagaacagg agatagtctt taacatgtag ggtaaaatct 36	0
aaggtagagg agagagcagc tgata atg ttt tta tgt gtt tgc tac ttt att 41  Met Phe Leu Cys Val Cys Tyr Phe Ile	
agg aag tot act too tto ttt too ata tot agt ag  Arg Lys Ser Thr Ser Phe Phe Ser Ile Ser Ser  5  1  5	1 <b>7</b>
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                                                                        49
     Met Gly Lys Pro Arg Gly Gly Glu Met Leu Glu Val Val Lys Thr
                          -40
                                              -35
gto too act tto act ttg gga ggg tgg aaa ggg act gct cct gtg tcc
                                                                        97
Val Ser Thr Phe Thr Leu Gly Gly Trp Lys Gly Thr Ala Pro Val Ser
                    -25
                                         -20
tgc gcc tgg tgg ctg ctt ctc cca gtt tgg aag ctg gga ggg cag ctt
                                                                       145
Cys Ala Trp Trp Leu Leu Pro Val Trp Lys Leu Gly Gln Leu
                -10
                                     -5
gag cgc agg aag aat cca aag gaa tac tgt ctt ggc tcc tgg gtg tgg
                                                                       193
Glu Arg Arg Lys Asn Pro Lys Glu Tyr Cys Leu Gly Ser Trp Val Trp
ctc agt cct cag ctg gct cca agg
                                                                       217
Leu Ser Pro Gln Leu Ala Pro Arg
<210> 685
<211> 132
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<221> sig_peptide
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                                                                       60
ategacattt teeeta atg etg att tte ace ttt att tet act ttg etg ttt
                                                                       112
                  Met Leu Ile Phe Thr Phe Ile Ser Thr Leu Leu Phe
                       -15
gta ttc ttg gga gtt gtg gg
                                                                      132
Val Phe Leu Gly Val Val
<210> 686
<211> 260
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<213> Homo sapiens
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<223> Von Heijne matrix
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 seq PGSGLCSMAAVQA/GN

<223> Von Heijne matrix

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atg gaa gtt ctt tcb mtt ccc aac tct ttc cag acc caa gca ctc tgg	119
Met Glu Val Leu Ser Xaa Pro Asn Ser Phe Gln Thr Gln Ala Leu Trp	167
-35 -30 -25	
gac tca ctc cat agt cca gga gtt cca ggt tcc gga tta tgt tcc atg	215
Asp Ser Leu His Ser Pro Gly Val Pro Gly Ser Gly Leu Cys Ser Met	-10
-20 -15 -10	
gca gca gtc caa gca gga aac caa gcc atc tac tct gcc tcg ggg	260
Ala Ala Val Gln Ala Gly Asn Gln Ala Ile Tyr Ser Ala Ser Gly	
5 10	
<210> 687	
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·	
<220>	
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score 3.59999990463257	
seq LLTQAGFPRRGEA/AP	
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cctgcagggg cgggacccca ggaggaggga gaggacagag ccactgcaga ggaccagact	120
gggaaaacaa cgatatggca ggagccagtc ttggggcccg cttctaccgg cagatcaaaa gacatccggg gctgggacag aaagaacaac ccggagccct ggaaccgcct gagccccaat	180
gaccaataca agtteettge agttteeact gactataaga agetgaagaa ggaceggeea	240
gacttetaag ceaggetggg etgeeagtge e atg eaa gee aca gee age eag	300 352
Met Gln Ala Thr Ala Ser Gln	332
-40	
ccc atc cac ttc ttc crs tcc tcc ccg cag gcc cca agg cat cac tcc	400
Pro Ile His Phe Phe Xaa Ser Ser Pro Gln Ala Pro Arg His His Ser	
-35 -30 -25 -20	
gge cae cet gte ceg eta etg ett aca cag gee ggg tte eea ege aga	448
Gly His Pro Val Pro Leu Leu Leu Thr Gln Ala Gly Phe Pro Arg	
ggg gag gct gct cca ccc cta ctc c	477
Gly Glu Ala Ala Pro Pro Leu Leu	473
1 5	
<210> 688	
<211> 107	
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<221> sig_peptide	
<222> 594	

score 3.59999990463257 seq LCTFTLNLTAVRT/IX

<400> 688 acac atg cga ggg tak aac tgh gtg ttc agg gtt ttc tct gaa agc ctg 49 Met Arg Gly Xaa Asn Xaa Val Phe Arg Val Phe Ser Glu Ser Leu -25 aag gga ttg tgt acw ttt aca ttg aac ttg act gca gtt aga acc att 97 Lys Gly Leu Cys Thr Phe Thr Leu Asn Leu Thr Ala Val Arg Thr Ile -15 arc cta gat .g 107 Xaa Leu Asp <210> 689 <211> 377 <212> DNA <213> Homo sapiens <220> ' <221> CDS <222> 258..377 <221> sig_peptide <222> 258..353 <223> Von Heijne matrix score 3.59999990463257 seq RLTISTXLSTSXX/FM <400> 689 aaacacaaca accagattce teetetaaag aageeeetgg gageacaget cateaceatg 60 gactggacct ggaggttcct ctttttggtg acagcagcta cagatgtcca gtcccaggtc 120 cagctggtgc aagtctgggt actgaggtga agaggcctgg gtcctcggtg aaggtctcct 180 gtaagacttc tggaggcacc ttcagtagta atgccatcac gtgggtgcga caggccctg 240 gacaagggct tgagtgg atg ggr agg atc atc ccc atg gtt gaa aaa gcg 290 Met Gly Arg Ile Ile Pro Met Val Glu Lys Ala -30gac acc gca cag aag ttc cag ggc aga ctc act att agt aca dkv cta 338 Asp Thr Ala Gln Lys Phe Gln Gly Arg Leu Thr Ile Ser Thr Xaa Leu -15 tcg acg agc asa gsc ttc atg gaa ctg agc agt ctg aga 377 Ser Thr Ser Xaa Xaa Phe Met Glu Leu Ser Ser Leu Arg -5 <210> 690 <211> 388 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 53..388 <221> sig_peptide <222> 53..253 <223> Von Heijne matrix score 3.59999990463257 seq IIMVFVFICFCYL/HY <400> 690 ataaattcag tagttacctt agtagacaaa tcatttgaac caagttgcgg ac atg aat 58 ctt gtt att tgt gtc cta ctt ttg tcc att tgg aaa aat aat tgc atg 106

Leu Val Ile Cys Val Leu Leu Ser Ile Trp Lys Asn Asn Cys Met

WO 99/53051 367 -65 -60 -55 -50 act aca aac caa acc aat gga tet tet act aca gga gat aaa eet gtt Thr Thr Asn Gln Thr Asn Gly Ser Ser Thr Thr Gly Asp Lys Pro Val -45 -40 gaa tca atg cag aca aaa ttg aac tac ctt aga aga aat cta ctc att Glu Ser Met Gln Thr Lys Leu Asn Tyr Leu Arg Arg Asn Leu Leu Ile -25 tta gtt ggt att atc atc atg gtt ttt gtc ttt atc tgt ttt tgt tat 250 Leu Val Gly Ile Ile Ile Met Val Phe Val Phe Ile Cys Phe Cys Tyr -15 -10 ctc cat tat aat tgt ctg agc gat gat gcg tcc aaa gca gga atg gtc 298 Leu His Tyr Asn Cys Leu Ser Asp Asp Ala Ser Lys Ala Gly Met Val 10 aag aaa aaa ggc ata gca gcc aag tca tct aaa aca tca ttc agt gaa. 346 Lys Lys Lys Gly Ile Ala Ala Lys Ser Ser Lys Thr Ser Phe Ser Glu 25 gec aag aca gec tet caa tge agt tea gaa aca caa ace ggg 388 Ala Lys Thr Ala Ser Gln Cys Ser Ser Glu Thr Gln Thr Gly 40 <210> 691 <211> 408 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 304..408 <221> sig_peptide <222> 304..387 <223> Von Heijne matrix score 3.59999990463257 seq IFFSLTLSGCKFS/KL <400> 691 cttgacttct gtgcactcac aggcttgatc aacaccacaa ggaagctgcc aaggccatcc totgaaacca cagooogago totatgttgg cocottttag coatggotgg aatggotgag 120 acacaggaca ccaagteect aggetgtaca cageactggg accetgggee etgeceatgg 180 aacaattttt tcctcctaaa tcttcaggcc tgtgatggga ggggctaccg caaaggtctc 240 tgacatgccc cagatacatt ttccctattg tcttggggat taacatttgg ctcctcgtta 300 ctt atg caa att tct gca gcc agc ttg aat ttc tcc tca aaa aat gga 348 Met Gln Ile Ser Ala Ala Ser Leu Asn Phe Ser Ser Lys Asn Gly -25 -20 att ttc ttt tct tta aca ttg tca ggc tgc aaa ttt tcc aaa ctt tta 396 Ile Phe Phe Ser Leu Thr Leu Ser Gly Cys Lys Phe Ser Lys Leu Leu -5 tgc cct ttt ggg 408 Cys Pro Phe Gly 5 <210> 692 <211> 322 <212> DNA <213> Homo sapiens <220>

<221> CDS <222> 106..321 <221> sig_peptide <222> 106..261

<223> Von Heijne matrix

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<221> misc_feature <222> 284..285 <223> n=a, g, c or t <400> 692 tgttacctgt gtgcatatat tatatctact taagttttat tctaaataag gagcttgtga 60 tarttgtttc cgttttgtaa ttagaaggta ttatatgttc ctatc atg att ttt gag 117 Met Ile Phe Glu cct gtg gtt ctg aaa cca gtg ttt cta aat att ttt ttc ttt tca cat 165 Pro Val Val Leu Lys Pro Val Phe Leu Asn Ile Phe Phe Phe Ser His -45 -35 cat gta ttt aca gtg ttt ttc agt ggt agt cat gtt gac atc ctg agt 213 His Val Phe Thr Val Phe Phe Ser Gly Ser His Val Asp Ile Leu Ser -25 -20 ege aca gtt ett gtt tgg gae tgt ett ett eet eet eet tee tte tte 261 . Arg Thr Val Leu Val Trp Asp Cys Leu Leu Pro Pro Pro Ser Phe Phe, -15 -10 -5 ctc ctt ctt ctt tct tcc tnn tcc ttv ctc ctc ctt vct dct tct 309 Leu Leu Leu Ser Ser Ser Xaa Ser Xaa Leu Leu Leu Xaa Xaa Ser 10 tcc tcc tcc cgg g 322 Ser Ser Ser Arg 20 <210> 693 <211> 153 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 93..152 <221> sig peptide <222> 93..134 <223> Von Heijne matrix score 3.59999990463257 seq LVPLLSHLLFKFT/WP <400> 693 cttttttagt aggggagctt gataatggaa aacagtatga ggaattgtca cactgtatga 60 gattttaaac taaggcataa gaatgaaacc gg atg tta gtt cct ctt tta tca 113 Met Leu Val Pro Leu Leu Ser cac ttg ctc ttc aag ttt acc tgg cca aaa tkg tcc cag g 153 His Leu Leu Phe Lys Phe Thr Trp Pro Lys Xaa Ser Gln -5 1 <210> 694 <211> 234 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 23...232

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PCT/IB99/00712

370 <213> Homo sapiens <220> <221> CDS <222> 8..151 <221> sig_peptide <222> 8..127 <223> Von Heijne matrix score 3.59999990463257 seq ITALSQSLQPLRK/LP <400> 696 agacaag atg gcg acg tcc gtg ggg cac cga tgt ctg gga tta ctg cac 49 Met Ala Thr Ser Val Gly His Arg Cys Leu Gly Leu Leu His -35 -30 ggg gtc gcg ccg tgg cgg agc agc ctc cat ccc tgt gag atc act gcc 97 Gly Val Ala Pro Trp Arg Ser Ser Leu His Pro Cys Glu Ile Thr Ala -25 -20 ctg age caa tee eta cag eee tta egg aag etg eet ttt aga gee tet 145 Leu Ser Gln Ser Leu Gln Pro Leu Arg Lys Leu Pro Phe Arg Ala Ser -5 ygc acg gg 153 Xaa Thr <210> 697 <211> 493 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 116..493 <221> sig_peptide <222> 116..262 <223> Von Heijne matrix score 3.59999990463257 seq YCLVTLVFFYSSA/SF <400> 697 aaaagctgac gacttcggtc tgcgccggaa gtgcatgagc tgccgatgtg gtgcttagtg 60 attgcggttt cggtcgctct cccgtgtttc ccgggctggg tatttgcctc gcacc atg 118 gcg ccc aag ggc aaa gtg ggc acg aga ggg aag aag cag ata ttt gaa 166 Ala Pro Lys Gly Lys Val Gly Thr Arg Gly Lys Lys Gln Ile Phe Glu gag aac aga gag act ctg aag ttc tac ctg cgg atc ata ctg ggg gcc 214 Glu Asn Arg Glu Thr Leu Lys Phe Tyr Leu Arg Ile Ile Leu Gly Ala -25 -20 aat gcc att tac tgc ctt gtg acg ttg gtc ttc ttt tac tca tct gcc 262 Asn Ala Ile Tyr Cys Leu Val Thr Leu Val Phe Phe Tyr Ser Ser Ala -15 -10 tea tit tgg gee tgg ttg gee etg gge tit agt etg gea gtg tat ggg 310 Ser Phe Trp Ala Trp Leu Ala Leu Gly Phe Ser Leu Ala Val Tyr Gly gcc agc tac cac tet atg agc teg atg gca cga gca gcg ttc tet gaq 358 Ala Ser Tyr His Ser Met Ser Ser Met Ala Arg Ala Ala Phe Ser Glu 20 gat ggg gcc ctg atg gat ggt ggc atg gac ctc aac atg gag cag ggc 406 Asp Gly Ala Leu Met Asp Gly Gly Met Asp Leu Asn Met Glu Gln Gly atg gca gag cac ctt aag gat gtk atc cta ctg aca gcc atc gtg caq

454

371 Met Ala Glu His Leu Lys Asp Val Ile Leu Leu Thr Ala Ile Val Gln 55 gtg ctc agc tgc ttc tct ctc tat gtc tgg tcc ttc tgg 493 Val Leu Ser Cys Phe Ser Leu Tyr Val Trp Ser Phe Trp 70 <210> 698 <211> 174 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 8..172 <221> sig peptide <222> 8..94 <223> Von Heijne matrix score 3.59999990463257 seq AFNKAVWFTPCSC/QE <400> 698 aacaaag atg gcg gcg gtg act gtg acg gtg acg aag acg gcg gcg 49 Met Ala Ala Val Thr Val Thr Val Thr Lys Thr Ala Ala Ala -25 -20 gcg acg gca ttt aac aag gcg gtg tgg ttt act cca tgc agt tgt cag 97 Ala Thr Ala Phe Asn Lys Ala Val Trp Phe Thr Pro Cys Ser Cys Gln -10 -5 gag gta agt agc agg ctg ccg gct cgg acg gcg acg cgg cag gac 145 Glu Val Ser Ser Arg Leu Pro Ala Arg Thr Ala Ala Thr Arg Gln Asp agg gcg gat aag aag gag cgg ccc tgt gg 174 Arg Ala Asp Lys Lys Glu Arg Pro Cys 20 <210> 699 <211> 300 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 199..300 <221> sig peptide <222> 199..255· <223> Von Heijne matrix score 3.59999990463257 seq PGSAICLWHSTLG/GX <221> misc_feature <222> 261 <223> n=a, g, c or t <400> 699 attttgtctc ggcagcggtg gccgwagctc catcgcattt tatgtttctg gcgagaaggg 60 aacggagttt tcatcaggta gattggtttt trtgcggccg tcctccaccg tttcctccag 120 gacagcacct agtcgtggcc ggaggagtct catagctgtc agaaagaata agactgattt 180 tatgggaaaa ttaagcag atg ctc cag ttt gag aaa cct gga tct gcg atc Met Leu Gln Phe Glu Lys Pro Gly Ser Ala Ile -15 -10 tgt ttg tgg cac agc act ttg gga ggy ymn ggc ggg cgt gag att gds

279

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372
Cys Leu Trp His Ser Thr Leu Gly Gly Xaa Gly Gly Arg Glu Ile Xaa
            - 5
                                 1
agt ttg aga cca gcc tgc ggg
                                                                       300
Ser Leu Arg Pro Ala Cys Gly
    10
<210> 700
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<222> 86..139
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      seg LAILLKWVSNSKS/FL
<400> 700
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acaaatagaa actattgatt ttygt atg ttg att tcg tat ctt gca att tta
                                                                       112
                            Met Leu Ile Ser Tyr Leu Ala Ile Leu
                                         -15
cta aaa tgg gtt agc aat tct aag agt ttt ttg gtg aag gca tcg gg
                                                                      159
Leu Lys Trp Val Ser Asn Ser Lys Ser Phe Leu Val Lys Ala Ser
                -5
<210> 701
<211> 274
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<213> Homo sapiens
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<221> CDS
<222> 46..273
<221> sig_peptide
<222> 46..90
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      score 3.59999990463257
      seq LQTLAFWSAYVPC/QT
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                                                   Met Lys Leu Gln
                                                   -15
acc ctc gca ttc tgg tca gcc tat gtg cca tgc cag acc cag gac cgg
                                                                      105
Thr Leu Ala Phe Trp Ser Ala Tyr Val Pro Cys Gln Thr Gln Asp Arg
gat gcc ccg cgc ctc acc ctg gag cag att gac ctc ata cgc cgc atg
                                                                      153
Asp Ala Pro Arg Leu Thr Leu Glu Gln Ile Asp Leu Ile Arg Arg Met
                10
                                    15
tgt gcc tcc tat tct gag ctg gag ctt gtg acc tcg gct aaa gct ctg
                                                                      201
Cys Ala Ser Tyr Ser Glu Leu Glu Leu Val Thr Ser Ala Lys Ala Leu
            25
aac gac act cag aaa ttg gcc tgc ctc atc ggt gta gag ggt ggc cac
                                                                      249
Asn Asp Thr Gln Lys Leu Ala Cys Leu Ile Gly Val Glu Gly Gly His
teg etg gac aat age etc tee agg g
                                                                      274
Ser Leu Asp Asn Ser Leu Ser Arg
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55
                         60
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<222>. 107..175
<221> sig_peptide
<222> 107..148
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                                                                        60
atttgatttt tcaagtgagt tattaggata taggtgggag tggaga atg cct gcc
                                                                       115
                                                    Met Pro Ala
tge ctt tet tee ttt gte att eee tet ete ett tet eee tee tee eet
                                                                       163
Cys Leu Ser Ser Phe Val Ile Pro Ser Leu Leu Ser Pro Ser Ser Pro
    -10
                         - 5
ccc tcc ata ggg
                                                                       175
Pro Ser Ile Gly
<210> 703
<211> 298
<212> DNA
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<220>
<221> CDS
<222> 197..298
<221> sig peptide
<222> 197..244
<223> Von Heijne matrix
      score 3.5
     seq SFAGSCTILGASS/HS
<400> 703
ttttcatgtg tctgttggct gcataaatgt cttcttctga gaagtgtctg ttcatatcct
                                                                        60
tegeceactt gttgatgagg ttgttttttt cttgtaaatt/ tgtttgtgtt cattgtaagt
                                                                       120
totggatatt agccotttgt cagatgagta gattgtaaaa attttctccc attctacagg
                                                                       180
ttgcctgttc actctg atg gta gtt tct ttt gct ggt tct tgc aca att cta
                                                                       232
                  Met Val Val Ser Phe Ala Gly Ser Cys Thr Ile Leu
ggc gcc agt agc cat tca ttc ccc att gaa gtc agc ctg ttc cca gtg
                                                                       280
Gly Ala Ser Ser His Ser Phe Pro Ile Glu Val Ser Leu Phe Pro Val
                                                     10
                                                                       298
gac tgt ggc ttc ctc ttg
Asp Cys Gly Phe Leu Leu
        15
<210> 704
<211> 136
<212> DNA
<213> Homo sapiens
<220>
<221> CDS
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374
<222> 41..136
<221> sig_peptide
<222> 41..100
<223> Von Heijne matrix
      score 3.5
      seq AVSQSWLAAPSTS/WV
<400> 704
ttcttattaa agatttattt ttgtagagac agatgtctca atg tgt tgc cca ggc
                                                                        55
                                             Met Cys Cys Pro Gly
tgg aac gca gtg tcg caa tet tgg etc get gea eet tee aec tee tgg
                                                                       103
Trp Asn Ala Val Ser Gln Ser Trp Leu Ala Ala Pro Ser Thr Ser Trp
-15
                    -10
gtt caa gag att ctc gta ctt cag cct cca ggg
                                                                       136
Val Gln Glu Ile Leu Val Leu Gln Pro Pro Gly
<210> 705
<211> 433
<212> DNA
<213> Homo sapiens
<220>
<221> CDS
<222> 225..431
<221> sig_peptide
<222> 225..386
<223> Von Heijne matrix
      score 3.5
      seq IRCPLIFLXXVSG/TX
agaggactay gcgagagcgt ctacggttgt gccaaaggaa aaaaaatgtt cctaagaaaa
                                                                       60
gagtatacaa agttgtgttc atcaaagtct ggaacccaaa ggtgtccctc caaagctgta
                                                                      120
cacgacagag aaaacgcgaa ctgaaagaag aagcaggtcc caaggggcca ggcgcctcct
                                                                      180
ccacctcctc ctcctcctag gattaacctc catttcagct aatc atg gga gag att
                                                                      236
                                                  Met Gly Glu Ile
aaa gtc tct cct gat tat aac tgg ttt aga ggt aca gtt ccc ctt aaa
                                                                      284
Lys Val Ser Pro Asp Tyr Asn Trp Phe Arg Gly Thr Val Pro Leu Lys
-50
                    -45
                                         -40
aab dtw atk gtg gat gat gat gac agt aag ata tgg tcg chc tat gac
                                                                      332
Xaa Xaa Xaa Val Asp Asp Asp Ser Lys Ile Trp Ser Xaa Tyr Asp
                -30
                                    -25
                                                         -20
gcg ggc ccc cga agt atc agg tgt cct ctc ata ttc ctg cyc yct gtc
                                                                      380
Ala Gly Pro Arg Ser Ile Arg Cys Pro Leu Ile Phe Leu Xaa Xaa Val
            -15
                                -10
agt gga act gha gat gtc ttt ttc cgg cag att ttg gct ctg act gga
                                                                      428
Ser Gly Thr Xaa Asp Val Phe Phe Arg Gln Ile Leu Ala Leu Thr Gly
tgg gg
                                                                      433
Trp
15
<210> 706
<211> 419
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<213> Homo sapiens
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<220> <221> CDS WO 99/53051 PCT/IB99/00712

. 375 <222> 284..418

<221> sig_peptide

<222> 284..331

<223> Von Heijne matrix score 3.5 seq SHSHLSLVGHSRA/CG

## <400> 706

attgaaaatc attaaaaatc ttagcaattg ttttaaatta tctaattttt ttctccaaat 60 aatatctatt ttagcagcca aatcaccaca aatcattggt ttttatcttt agttgtgggt 120 gcacagcggg tgcgtgtatt ttggggcatg tgaggtgtct tgatgcgttc atgcagtgtg 180 taacagtcac atcagggtaa atgggacatc tttcacctca agcatttatc cttcgtgtta 240 tggacaccct cagctggaaa ggggggctgc gtcgtgagta tga atg gat gca agt 295 Met Asp Ala Ser

cat agc cac ctg agc ctg gtg ggg cac agc agg gcc tgt gga gtc aca 343
His Ser His Leu Ser Leu Val Gly His Ser Arg Ala Cys Gly Val Thr

-10 -5 1
tcc cgg cct cat gct cgg cat agg gga cgc tgc tta ggt cca tgc agt 391
Ser Arg Pro His Ala Arg His Arg Gly Arg Cys Leu Gly Pro Cys Ser
5 10 15 20

cgc tca ggg ccc agg ctg tgc agc gcc a
Arg Ser Gly Pro Arg Leu Cys Ser Ala

25

<210> 707

<211> 382

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> 200..382

<221> sig peptide

<222> 200..301

<223> Von Heijne matrix
 score 3.5
 seq LISHDPWPRGAFA/LS

<221> misc_feature

-5

<222> 365

<223> n=a, g, c or t

## <400> 707

gttacttatg gttgagagag aatatttttc agattttatt ggacattgat atttgtaaat 60 tgttcattcc ttttgcccag ttttctattg agtggttcat agtttctcat gggtatccaa 120 gagttctgga tatgtagagg tggagggtca atctcatcay ttccttgttt taaaaatctt 180 ccatggtttt gtcatcact atg ggc tca aac gcc gtg gtg tgg cat aca aag 232 Met Gly Ser Asn Ala Val Val Trp His Thr Lys

-30 -25

328

376

ccc tca ctt ctg aac cac cct gct tcc agc ctc atc tcc cat gat ccc
Pro Ser Leu Leu Asn His Pro Ala Ser Ser Leu Ile Ser His Asp Pro
-20
-15
-10

-20 -15 -10
tgg cca cgc ggt gcg ttt gcg ctt tca tgt cca agt gct tcc ttc atg
Trp Pro Arg Gly Ala Phe Ala Leu Ser Cys Pro Ser Ala Ser Phe Met

ttg ttt tct tcc tta caa tgc cct ttc cct tat tgd naa aca gag tgc Leu Phe Ser Ser Leu Gln Cys Pro Phe Pro Tyr Xaa Xaa Thr Glu Cys 10 15 20 25

aac gwg

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Asn Xaa
<210> 708
<211> 384
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<213> Homo sapiens
<220>
<221> CDS
<222> 215..382
<221> sig_peptide
<222> 215..268
<223> Von Heijne matrix
      score 3.5
      seq ACLFRAVADQVYG/DQ
<400> 708
aagtgacget acaggggcca getatgetee egggagtgtt gatgttttee agteatteeg
                                                                        60
gctqacagcg ttcaagttgg aatcctggag gggaggtgtt tttcctgtcg tacgtgggac
                                                                       120
aggecacget gteegteege agtacegacg cetgeageag gageattggt ttgaaaagge
                                                                       180
cctacgagac aagaagggct tcatcatcaa gcag atg aag gag gat ggc gcc tgt
                                                                       235
                                      Met Lys Glu Asp Gly Ala Cys
etc ttc egg get gta get gac eag gtg tat gga gac eag gac atg eat
                                                                       283
Leu Phe Arg Ala Val Ala Asp Gln Val Tyr Gly Asp Gln Asp Met His
gag gtt gtg cga aag cat trc atg gac tat ctg atg aag aat gcc gac
                                                                       331
Glu Val Val Arg Lys His Xaa Met Asp Tyr Leu Met Lys Asn Ala Asp
                                   .. 15
tay ttc tcc arc.tat gtc aca gag gac ttt acc acc tac att akc agg
                                                                       379
Tyr Phe Ser Xaa Tyr Val Thr Glu Asp Phe Thr Thr Tyr Ile Xaa Arg
aag cg
                                                                       384
Lys
<210> 709
<211> 149
<212> DNA
<213> Homo sapiens
<220>
<221> CDS
<222> 76..147
<221> sig_peptide
<222> 76..138
<223> Von Heijne matrix
      score 3.5
      seq VLIMIXEAXNVWC/GD
<221> misc_feature
<222> 123..124
<223> n=a, g, c or t
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acctaatatt aaaaatette ttetetaaaa gtggcatata accetgatea agaggteatg
                                                                        60
ggctcagttt gatat atg gtt cac ctc att ctt act gaa gtc ctc att atg
                                                                       111
                 Met Val His Leu Ile Leu Thr Glu Val Leu Ile Met
                     ~20
                                          ~15
atc akc gag gcn nsg aat gtg tgg tgt ggg gat tcg gg
                                                                       149
Ile Xaa Glu Ala Xaa Asn Val Trp Cys Gly Asp Ser
```

-5 1

<210> 710 <211> 167 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 15..167 <221> sig_peptide <222> 15..155 <223> Von Heijne matrix score 3.5 seq CLXFGILASEVYS/WN <400> 710 atatttcatg gcga atg tac cac aat tta ttt gct ctg ttg ttg ata gac 50 Met Tyr His Asn Leu Phe Ala Leu Leu Leu Ile Asp, . -45 -40 att cat gtt gtt cta gtt ttt tac tgc ctg gat ctc tta atg att cat 98 Ile His Val Val Leu Val Phe Tyr Cys Leu Asp Leu Leu Met Ile His -30 -35 -25 att ttc tat tgt aaa tac tgc ctt gka ttt ggk att tta gca agt gaa 146 Ile Phe Tyr Cys Lys Tyr Cys Leu Xaa Phe Gly Ile Leu Ala Ser Glu -15 -10 gtc tat tct tgg aac att tac 167 Val Tyr Ser Trp Asn Ile Tyr <210> 711 <211> 215 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 84..215 <221> sig_peptide <222> 84..170 <223> Von Heijne matrix score 3.5 seq SPLCSXSSGYCXA/FP <400> 711 ccgcttttgg ctgcatcagc cggggattgc cggcgccagg tgctgggggc gactcggaca 60 gegggagegt ggggtggagt agg atg gag tet eee tee ega get ggg ggt gtr 113 Met Glu Ser Pro Ser Arg Ala Gly Gly Val -25 grc ctm vga aag gct gct tcg ccg ctg tgt tcg gmv agc tct gga tac 161 " Xaa Leu Xaa Lys Ala Ala Ser Pro Leu Cys Ser Xaa Ser Ser Gly Tyr -15 -10 tgc rgg gct ttt ccg cgg agg agc gcc cgc cgg cat ctg cat ccg gga 209 Cys Xaa Ala Phe Pro Arg Arg Ser Ala Arg Arg His Leu His Pro Gly cac ggg 215 His Gly 15

<210> 712

<211> 241

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<212> DNA
<213> Homo sapiens
<220>
<221> CDS
<222> 59..241
<221> sig peptide
<222> 59..133
<223> Von Heijne matrix
      score 3.5
      seq LISLSVLMPVQHS/PD
<400> 712
actateettt eeteattgaa ttgetgtgat acetttgttg caaatcaget gtetgeag
                                                                        58
atg tgg agg tat gtt tct aga ctt tct tct gtt cca ttg atc agc ttg
                                                                       106
Met Trp Arg Tyr Val Ser Arg Leu Ser Ser Val Pro Leu Ile Ser Leu
-25
                    -20
                                         -15
tet gte ttg atg eca gta cag eac tee eet gat ttt tgt age ttt att
                                                                       154
Ser Val Leu Met Pro Val Gln His Ser Pro Asp Phe Cys Ser Phe Ile
                -5
gta agt aca gtt atc cct tgg ttt cct tgg gga att ggt tcc agg acc
                                                                       202
Val Ser Thr Val Ile Pro Trp Phe Pro Trp Gly Ile Gly Ser Arg Thr
                            15
ctc atg gat ata aaa atc ctg gga tgc tcg agt cca ggg
                                                                       241
Leu Met Asp Ile Lys Ile Leu Gly Cys Ser Ser Pro Gly
    25
                        30
<210> 713
<211> 376
<212> DNA
<213> Homo sapiens
<220>
<221> CDS
<222> 276..374
<221> sig_peptide
<222> 276..365
<223> Von Heijne matrix
      score 3.5
      seq NLLKLSSHSPTCA/CK
<221> misc_feature
<222> 154,217
<223> n=a, g, c or t
<400> 713
tatgtacatt tgtcaaaact cagaaaatgt atatataata tgtgtgcata tgattttaag
                                                                       60
tagttttaca taaaaagata agcaaatatt ggatgctggt taacactaag catgctgaaa
                                                                       120
tatttagagg gaagagtatt attgtctaca atyngcttta aagacaccaa aaataaggtg
                                                                       180
grttaattwa wkggsywwgg grmdwtggat aaatggnkag awatgtgata aagcaagtct
                                                                      240
aatagaattt tgtggcagaa tctaatggcg gctat atg gat gtt agc tgt aaa
                                                                      293
                                        Met Asp Val Ser Cys Lys
                                        -30
att ctt tac aat gtg att gaa aaa ttt tgc aat aat ctg ttg aag ctt
                                                                       341
Ile Leu Tyr Asn Val Ile Glu Lys Phe Cys Asn Asn Leu Leu Lys Leu
                -20
                                     -15
tct tcc cat tcc cct act tgt gct tgc aaa cta aa
                                                                      376
Ser Ser His Ser Pro Thr Cys Ala Cys Lys Leu
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379

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<210> 714
<211> 304
<212> DNA
<213> Homo sapiens
<220>
<221> CDS
<222> 216..302
<221> sig_peptide
<222> 216..275
<223> Von Heijne matrix
     score 3.5
      seq SHLSGSSLQLCVA/QF
<400> 714
gtatgtgtga tttgatttta tttgcccttt gaactatgac ccaatactcc ccaaacctgt .
tattcagttt ttgcccagag ttattatatc tggggaataa acagaggaca cacacccaga
                                                                   120
ggctgccagt agcaaaaatc actgtaattc aaaaagcatg acactacggt agtgaaatta
                                                                    180
tcacactttt ctttgcatag agcagtttac ttgtg atg att ttc aaa gat gtg
                                                                    233
                                      Met Ile Phe Lys Asp Val
                                      -20
ttc tcc cac ttg tca ggt tca tct ctt caa ctg tgt gtc gca caa ttt
                                                                    281
Phe Ser His Leu Ser Gly Ser Ser Leu Gln Leu Cys Val Ala Gln Phe
               -10
ctc gaw ctc agt gct gtt gac at
                                                                    304
Leu Xaa Leu Ser Ala Val Asp
<210> 715
<211> 242
<212> DNA
<213> Homo sapiens
<220>
<221> CDS
<222> 91..240
<221> sig_peptide
<222> 91..222
<223> Von Heijne matrix
     score 3.5
     seq SFSFLFFFFLSFF/FF
<400> 715
gtttgtgatt aagtgatttc ctctagtggt atgctttgac tcctctttag cttttgtgta
                                                                    60
aatactatag gtttttgctt tgtggttaac atg aag ctt aca aaa aat atc tta
                                                                   114
                               Met Lys Leu Thr Lys Asn Ile Leu
twa gta ata ata ggc tgt ttt aag ctg ata gcc tac aaa aac tct gta
                                                                   162
Xaa Val Ile Ile Gly Cys Phe Lys Leu Ile Ala Tyr Lys Asn Ser Val
                       -30
ctg tac ttt tac tct aac ttc tca ttt tct ttt ctt ttc ttt ttc
Leu Tyr Phe Tyr Ser Asn Phe Ser Phe Ser Phe Leu Phe Phe Phe
-20
                   -15
                                       -10
242
Leu Ser Phe Phe Phe Phe Phe Phe Phe
               1
<210> 716
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<211> 375

<212> DNA

<213> Homo sapiens

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<222> 100375			
<221> sig_peptide			
<222> 100360			•
<223> Von Heijne matrix			
score 3.5		•	•
seg VAGXMLAPGGTLA/	/DD		
•			
<400> 716		•	
ctggcgtyag ttccggtcgc ag	naggagaca ccgcc	gcagt tgccggtaca	tcqqqqattt 60
etggetettt cetettegee ti			
55	33 3 3	Met Asn Asn	_
		-85	<b>4</b> . '
cag caw rag cca acg cta	tca qqc caq cq	t ttt aaa act aga	a aaa aga 162
Gln Xaa Xaa Pro Thr Leu			
-80	-75	-70	, , ,
gat gaa aaa gag agg ttt	gac cct act ca	ttt caa gac tgt	att att 210
Asp Glu Lys Glu Arg Phe			
	-60	-55	
caa ggc tta act gaa acc	ggt act gat tt	g qaa qca qta qct	aag ttt 258
Gln Gly Leu Thr Glu Thr	Gly Thr Asp Le	u Glu Ala Val Ala	Lys Phe
-50 -45	-	-40	-35
ctt gat gct tct gga gca	aaa ctt gat ta	c cgt cga tat gca	gaa aca 306
Leu Asp Ala Ser Gly Ala			
-30	-2		-20
ctc ttt gac att ctg gtg	gct ggt kga at	g ctg gcc cca ggt	ggt aca 354
Leu Phe Asp Ile Leu Val	Ala Gly Xaa Me	Leu Ala Pro Gly	Gly Thr
-15	-10	-5	•
ctg gca gat gac atg atg	cvg		375
Leu Ala Asp Asp Met Met	Xaa		
1	5		
	•		
<210> 717			
<211> 429			
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<220>			
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<222> 324428			
<221> sig_peptide			
<222> 324374	•		
<223> Von Heijne matrix			
score 3.5			
seq LEIKLPFLPFAQQ/	ID ·		
<400> 717			
aacagtctat ttctgtttgt aa			
tateetttea ttetettagg tt			
atagtttcaa aatcttttat ct			
cccaattgtc aattggacat cc			
ccaagtetgt atcacttetg ge			
ccagtaacaa actagctgtg at			
	_	Ser Leu Glu Ile I	
	-15		10
ttt tta ccc ttt gca cag	caa att gac at	aaa too tgt tto	tac ttt 401
Phe Leu Pro Phe Ala Gln			Tyr Phe
. <b>-5</b>	1	5	
ttt ttt ttw aac wat kgc	ttc cct agg g		429

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Phe Phe Xaa Asn Xaa Xaa Phe Pro Arg
<210> 718
<211> 350
<212> DNA
<213> Homo sapiens
<220>
<221> CDS
<222> 4..348
<221> sig_peptide
<222> 4..108
<223> Von Heijne matrix
     score 3.5
      seq ATAAATAASATTG/AS
<221> misc_feature
<222> 155
<223> n=a, g, c or t
<400> 718
tga atg gac aga aaa tgg acc tgg aag aga ggg caa agg tca cat ctg
    Met Asp Arg Lys Trp Thr Trp Lys Arg Gly Gln Arg Ser His Leu
                        -30
gag toa ggc cag gct gcc ccg gcc act gca gca gct acg gca gca tct
                                                                       96
Glu Ser Gly Gln Ala Ala Pro Ala Thr Ala Ala Thr Ala Ala Ser
                    -15
                                        -10
gcc aca acg ggg gca agt gtg tgg aga agc aca atg ggc wac ctg tgt
                                                                      144
Ala Thr Thr Gly Ala Ser Val Trp Arg Ser Thr Met Gly Xaa Leu Cys
gat tgc acc anb dca cct tat gaa ggg ccc ttt tgc aaa aaa gag gtt
                                                                      192
Asp Cys Thr Xaa Xaa Pro Tyr Glu Gly Pro Phe Cys Lys Lys Glu Val
tet get gtt ttt gag get gge acg teg gtt act tac atg ttt caa gaa
                                                                      240
Ser Ala Val Phe Glu Ala Gly Thr Ser Val Thr Tyr Met Phe Gln Glu
                        35
ccc tat cct gtg acc aag aat ata agc ctc tca tcc tca gct att tac
                                                                      288
Pro Tyr Pro Val Thr Lys Asn Ile Ser Leu Ser Ser Ser Ala Ile Tyr
                    50
aca gat tca gct cca tcc aag gaa aac att gca ctt agc ttt gtg aca
                                                                      336
Thr Asp Ser Ala Pro Ser Lys Glu Asn Ile Ala Leu Ser Phe Val Thr
acc caa gca ccg gg
                                                                      350
Thr Gln Ala Pro
            80
<210> 719
<211> 305
<212> DNA
<213> Homo sapiens
<220>
<221> CDS
<222> 84..305
<221> sig_peptide
<222> 84..212
<223> Von Heijne matrix
      score 3.5
      seq VLSIKHLPPQLRA/FQ
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<221> sig_peptide
<222> 217..306
<223> Von Heijne matrix
      score 3.5
      seq FLFFLQFSFPLYY/LF
<221> misc feature
. <222> 316,319
\langle 223 \rangle n=a, g, c or t,
<400> 721
ggcatgttta tatactcatt ccctggtgat tgtattttgc atacttgatt tttacctaag-
cattlatett titteettta tittetgitg ettigtetti tigtaatgee teetggggea
atttetttga tttttatett geagttette tattgagttt tgeatgttgg etateatgtt
                                                                        180
ttaaattttc atttttcata gtattctgtc ctatgg atg ttt cat ggc tgt cat
                                         Met Phe His Gly Cys His
                                          -30
att tta tct ttt ctg agg ata tca act aga ggt ttt ctt ttt ttt ctt
                                                                        282
Ile Leu Ser Phe Leu Arg Ile Ser Thr Arg Gly Phe Leu Phe Phe Leu
                 -20
                                      -15
caa ttt tcc ttt cct ctg tat tat ctc ttt cgg ngg ntt ttc cct caq
                                                                        330
Gln Phe Ser Phe Pro Leu Tyr Tyr Leu Phe Arg Xaa Xaa Phe Pro Gln
             -5
tct ttc atg ttg gag gca ttt gtc aga tgt
                                                                        360
Ser Phe Met Leu Glu Ala Phe Val Arg Cys
<210> 722
<211> 191
<212> DNA
<213> Homo sapiens
<220>
<221> CDS
<222> 64...189
<221> sig_peptide
<222> 64..141
<223> Von Heijne matrix
      score 3.5
      seq LVLYAPWVPPLLL/AF
<400> 722
ttctcctctt gtgaaggcag ctcctcagat ccagggagta tctgcacgga cctcatttat
                                                                         60
gtt atg tat aga cat tcc aaa cag cgt aat aat gtc cca tgc ctt gta
                                                                        108
    Met Tyr Arg His Ser Lys Gln Arg Asn Asn Val Pro Cys Leu Val
        -25
                             -20
ctc tac gcc cct tgg gtc cct ccc ctc ctc cta gct ttc tgg ggc tgg
                                                                        156
Leu Tyr Ala Pro Trp Val Pro Pro Leu Leu Leu Ala Phe Trp Gly Trp
                         -5
tgg ctc ctg gag cag ggt ctt ttt ttt ttt ttt tt
                                                                        191
Trp Leu Leu Glu Gln Gly Leu Phe Phe Phe
                 10
<210> 723
<211> 473
<212> DNA
<213> Homo sapiens
<220>
<221> CDS
<222> 63..473
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<221> sig_peptide <222> 63..212 <223> Von Heijne matrix score 3.5 seq ITYGVFLCIDCSG/SH <400> 723 tttttttttc gtcgactctt accggttggc tgggccagct gcgccgcggc tcacagctga 60 cg atg ggg gac ccc agc aag cag gac atc ttg acc atc ttc aag cgc 107 Met Gly Asp Pro Ser Lys Gln Asp Ile Leu Thr Ile Phe Lys Arq -45 ctc cgc tcg gtg ccc act aac aag gtg tgt ttt gat tgt ggt gcc aaa 155 Leu Arg Ser Val Pro Thr Asn Lys Val Cys Phe Asp Cys Gly Ala Lys -35 -30 -25 aat ccc agc tgg gca agc ata acc tat gga gtg ttc ctt tgc att gat 203 Asn Pro Ser Trp Ala Ser Ile Thr Tyr Gly Val Phe Leu Cys Ile Asp -10 tgc tca ggg tcc cac cgg tca ctt ggt gtt cac ttg agt ttt att cga 251 Cys Ser Gly Ser His Arg Ser Leu Gly Val His Leu Ser Phe Ile Arg tot aca gag ttg gat too aac tgg tca tgg tit cag ttg cga tgc atg 299 Ser Thr Glu Leu Asp Ser Asn Trp Ser Trp Phe Gln Leu Arg Cys Met caa gtc gga gga aac gct agt gca tct tcc ttt ttt cat caa cat ggg 347 Gln Val Gly Gly Asn Ala Ser Ala Ser Ser Phe Phe His Gln His Gly tgt tcc acc aat gac acc aat gcc aag tac aac agt cgt gct gct cag 395 Cys Ser Thr Asn Asp Thr Asn Ala Lys Tyr Asn Ser Arg Ala Ala Gln 55 ctc tat agg gag aaa atc aaa tcg ctc gcc tct caa gca aca cgg aag 443 Leu Tyr Arg Glu Lys Ile Lys Ser Leu Ala Ser Gln Ala Thr Arg Lys 65 cat ggc act gat ctg tgg ctt gat agt tgt 473 His Gly Thr Asp Leu Trp Leu Asp Ser Cys <210> 724 <211> 139 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 60..137 <221> sig peptide <222> 60..125 <223> Von Heijne matrix score 3.5 seq LLLHLVFHQRTLI/SL <400> 724 tttagcattc aagccgtgat tagtgctttc tcttctcccc agcctgcctt tcagaacag 59 atg cct ctc cct ccc aat cag tcc cct cta ctg ctg cac ctg gtg ttt 107 Met Pro Leu Pro Pro Asn Gln Ser Pro Leu Leu His Leu Val Phe -20 -15 cat caa agg acc ctg att tcc ctc ccg ccg cc 139 His Gln Arg Thr Leu Ile Ser Leu Pro Pro -5 1 <210> 725 <211> 187

<212> DNA <213> Homo sapiens	
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tgt aat gat ggg aag ggh wga gsm tca gwg gtg ctt gga ttg gaa caa Cys Asn Asp Gly Lys Gly Xaa Xaa Ser Xaa Val Leu Gly Leu Glu Gln 10 15 20	152
Xaa Leu Pro Glu Ser Ala Gly Met Val Xaa Phe Leu Gly Leu Lys His 25 30 35 40	200
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                                                                      104
Val Leu Trp Ala Gly Pro Xaa Val Pro Leu Cys Ala Ala Xaa Gly
ctt ggt gcc ctg cat ccc aga tgc tct agt caa ggc ttg agg ctt gcr
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Leu Gly Ala Leu His Pro Arg Cys Ser Ser Gln Gly Leu Arg Leu Ala
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ttctaccctc aggtgmtc atg aat tgg agg cgg aaa agt gtc att ggt ctg
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                  Met Asn Trp Arg Arg Lys Ser Val Ile Gly Leu
                        -40
age tte gae tte gtg get etg aac etg aeg gge tte gtg gee tae agt
                                                                      219
Ser Phe Asp Phe Val Ala Leu Asn Leu Thr Gly Phe Val Ala Tyr Ser
-30
                    -25
                                        -20
gta ttc aac atc ggc ctc ctc tgg gtg ccc twc wtc daa gga gca gtt
                                                                      267
Val Phe Asn Ile Gly Leu Leu Trp Val Pro Xaa Xaa Xaa Gly Ala Val
                -10
                                     -5
tet eet caa ata eee caa egg agt gaa eee egt gaa eag caa ega egt
                                                                      315
Ser Pro Gln Ile Pro Gln Arg Ser Glu Pro Arg Glu Gln Gln Arg Arg
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Leu Leu
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Phe His Glu Ile His Ser Thr Gly Ser Glu Pro Pro Leu Leu Ile Met 80 85 90	•
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gaa sac aag agc tct tct ctg ttc gac atg gcc caa ttc gag cgg cta Glu Xaa Lys Ser Ser Ser Leu Phe Asp Met Ala Gln Phe Glu Arg Leu 115 120 125	447
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aac acc gcc ttg cag tcc gtt tct ctt cga agt aag aca acc atc cgg Asn Thr Ala Leu Gln Ser Val Ser Leu Arg Ser Lys Thr Thr Ile Arg 30 35 40	329
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gag cat ttt tca gga gca gta tat gaa gga caa ttt aag gat aat atg Glu His Phe Ser Gly Ala Val Tyr Glu Gly Gln Phe Lys Asp Asn Met	342
ttt cat gga ctg ggg act tac aca ttc cca aat ggg gca aag tat act Phe His Gly Leu Gly Thr Tyr Thr Phe Pro Asn Gly Ala Lys Tyr Thr 25 30 35	390
gga att tc Gly Ile	398

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40

313

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Phe Asp Thr Val Phe Gly Pro Glu Ser Lys Gln Leu Asp Val Tyr Asn
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cct ggg gag gac aga ttc aaa cct gtg gta cca tgg cct cat gtt gaa
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Pro Gly Glu Asp Arg Phe Lys Pro Val Val Pro Trp Pro His Val Glu
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                                                                       110
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Val Ser Lys Ser Asn Lys Lys Arg Ile Asn Leu Cys Asn Gly Phe Trp
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Asn Glu Lys Ile Lys Asn Arg
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tgt agc agt cta ctc acg gcc cct gta ctt tgc tac tgg agg gcc Cys Ser Ser Leu Leu Thr Ala Pro Val Leu Cys Tyr Trp Arg Ala 30 35 40	
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gta tta tta aac aca tgc tta tat gta cct tat ggg tat ttg tca Val Leu Leu Asn Thr Cys Leu Tyr Val Pro Tyr Gly Tyr Leu Ser 20 25 30	ctt 158
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	Ser 15
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Glu Thr Leu Lys Glu Glu Ser	Gln Ser Arg His Val Leu Pro Ala 20	Ser 25									
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Phe Glu Val Asn Ser Leu Gln 30	Lys Ser Asn Trp Gly Phe Leu Leu 35 40	Thr									
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Gly Ser Leu Val Asp İle Gly	agt ggg gac gga'cgc att gtc ata Ser Gly Asp Gly Arg Ile Val Ile	Ala									
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Leu Trp Gly Pro Tyr Lys Asp 15	Ile Trp His Lys Val Gly Asn Ala 20 25	Leu									
	gtt cam ctt ctt gat aag att ttg Val Xaa Leu Leu Asp Lys Ile Leu 40										
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	Gln Lys Ala Ser Thr Glu Gly Val										

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                                 85
gaa gcc ttt att ctc agt gac ctt ttt gat att gga gaa ttg gca gct
                                                                       338
Glu Ala Phe Ile Leu Ser Asp Leu Phe Asp Ile Gly Glu Leu Ala Ala
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Val Glu Leu Leu Ala Gly Glu His Gln Gln Pro His Phe Pro Gly
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                                                                      508
Glu Glu Glu Arg Arg Val Phe Ala Glu Cys Asn Asp Glu Ser Phe Trp
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Phe Arg Ser Val Pro Leu Ala Ala Thr Ser Met Leu Ile Thr Gln Gly
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Leu Ile Ser Lys Gly Ile Leu Ser Ser His Pro Lys Tyr Gly Ser Ile
cct aaa ctt ata ctt gct tgt atc atg gga tac ttt gct gga aaa ctt
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Pro Lys Leu Ile Leu Ala Cys Ile Met Gly Tyr Phe Ala Gly Lys Leu
tct tat gtg aaa act tgc caa gag aaa ttc aag aaa ctt gaa aat tcc
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Ser Tyr Val Lys Thr Cys Gln Glu Lys Phe Lys Lys Leu Glu Asn Ser
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Pro
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                                                           Met His
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Leu
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                                                                      111
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Val Pro Ser Asp Ser Gln Ala Arg Glu Lys Leu Ala Leu Tyr Val Tyr
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Glu Tyr Leu Leu His Val Gly Ala Gln Lys Ser Ala Gln Thr Phe Leu
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Ser Glu Ile Arg Trp Glu Lys Asn Ile Thr Leu Gly Glu Pro Pro Gly
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Pro Glu Arg Arg Glu Thr Cys Glu His Ser Ser Glu Ala Lys Ala Phe
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His Asp Tyr Ser Ala Ala Ala Pro Ser Pro Val Leu Gly Asn Ile
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                         Met Asn Pro Glu Tyr Asp Tyr Leu Phe Lys
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Leu Leu Leu Ile Gly Asp Ser Gly Val Gly Lys Ser Cys Leu Leu
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                                                                      208
Arg Phe Ala Asp Asp Thr Tyr Thr Glu Ser Tyr Ile Ser Thr Ile Gly
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gtg gac ttc aag atc cga acc atc gag ctg gat ggc aaa act atc aaa
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Val Asp Phe Lys Ile Arg Thr Ile Glu Leu Asp Gly Lys Thr Ile Lys
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Leu Gln Ile Trp Asp Thr Ala Gly Gln Glu Arg Phe Arg Thr Ile Thr
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tcc age tac tac egg ggg gct cat ggc atc atc gtg gtg tat gac gtc
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Ser Ser Tyr Tyr Arg Gly Ala His Gly Ile Ile Val Val Tyr Asp Val
                    80
                                        85
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Thr Asp Gln Glu Ser Tyr Ala Xaa Val Lys Gln Trp Leu Gln Glu Ile
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gac c
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                                                                      300
tgtgttgtaa tgggctttta cgtcctgttt ataaa atg aat tcc aaa gca scc
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                                       Met Asn Ser Lys Ala Xaa
aag tca tca act gcc aac caa ggg gac ggg gat gaa gaa nct gtt ggg
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113

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cag atg ctc aag gag gga gcg aaa cac ttt tca gga tta gaa gag gct Gln Met Leu Lys Glu Gly Ala Lys His Phe Ser Gly Leu Glu Glu Ala 15 20 25	159
gtg tat aga aac ata caa gct tgc aag gag ctt gcc caa acc act cgt Val Tyr Arg Asn Ile Gln Ala Cys Lys Glu Leu Ala Gln Thr Thr Arg 30 35 40	207
aca gca tat gga cca aat gga atg aac aaa atg gtt atc aac cac ttg Thr Ala Tyr Gly Pro Asn Gly Met Asn Lys Met Val Ile Asn His Leu 45 50 55 60	255
gag aag ttg ttt gtg aca aac gat gca gca act att tta aga gaa cta Glu Lys Leu Phe Val Thr Asn Asp Ala Ala Thr Ile Leu Arg Glu Leu 65 70 75	303
gaa gta cag cat cct gct gca aaa atg att gta atg gct tct cat atg Glu Val Gln His Pro Ala Ala Lys Met Ile Val Met Ala Ser His Met 80 85 90	351
caa gag caa gaa gtt gga gat ggc aca aac ttt gtt ctg gta ttt gct Gln Glu Gln Glu Val Gly Asp Gly Thr Asn Phe Val Leu Val Phe Ala 95 100 105	399

Val Ser Glu Val

125

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Met Met Glu Glu Ser Gly

362

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15 gct gct act gct atg tct tct acc cct gtt cca tta gcg gca acc agt 271 Ala Ala Thr Ala Met Ser Ser Thr Pro Val Pro Leu Ala Ala Thr Ser

30 tot tot tot coa aat gta too too atg gag too tto coa coa cto 319 Ser Phe Ser Ser Pro Asn Val Ser Ser Met Glu Ser Phe Pro Pro Leu

45 gca tac tct act cct cag ccg ccc ctt cct cct gtg agg cct t

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<211> 368.

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gga gcc aaa ga Gly Ala Lys As 10	gag tgt a	aat gtg gta gaa Asn Val Val Glu 15	gtt gtg gcc cgg aac cat Val Val Ala Arg Asn His	284
gac cat cag gag Asp His Gln Glu 25	g atc gca g ı Ile Ala V	gtc cct gtg gcc	aan ctc aag ctg tcc tgc Xaa Leu Lys Leu Ser Cys 35	332
caa ccc atg cto Gln Pro Met Leo 40	ser Leu A		ctc caa	368
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aag cgt gat ctg Lys Arg Asp Leu 10 gaa ttt gat gaa Glu Phe Asp Glu 25 aca tct gag aag Thr Ser Glu Lys 40 gca gga gcc tct Ala Gly Ala Ser 55 aga tat gat ctc	ctc ttc con Leu Phe Good Ctg tgt con Leu Cys P	caa gcc ctg ggc Sin Ala Leu Gly 15 ctt gaa ttt ggt Phe Glu Phe Gly 30 cta agt aaa gaa cle Ser Lys Glu 5 ctt ctt tac aaa Val Leu Tyr Lys	Met Pro Thr Val Ser Val  1 5  cgc acc tac act gac gaa Arg Thr Tyr Thr Asp Glu 20  ctg gag ctt gat gaa att Leu Glu Leu Asp Glu Ile 35  caa ggt aat gta aag gca Gln Gly Asn Val Lys Ala 50  att gac gtc cct gcc aat Ile Asp Val Pro Ala Asn	101 149 197
aag cgt gat ctg Lys Arg Asp Leu 10 gaa ttt gat gaa Glu Phe Asp Glu 25 aca tct gag aag Thr Ser Glu Lys 40 gca gga gcc tct Ala Gly Ala Ser 55 aga tat gat ctc Arg Tyr Asp Leu ttc aaa gaa agg	ctc ttc c Leu Phe G cta tgt t Leu Cys P gaa ata a Glu Ile I gat gtt g Asp Val V 60 ctg tgt c Leu Cys L 75 ata aag g	caa gcc ctg ggc Sin Ala Leu Gly 15 Itt gaa ttt ggt Phe Glu Phe Gly 30 Ita agt aaa gaa Ile Ser Lys Glu Itt ctt tac aaa Val Leu Tyr Lys Itg gaa gga ttg Eu Glu Gly Leu 80 Ict cca gtg tat	Met Pro Thr Val Ser Val  Cgc acc tac act gac gaa Arg Thr Tyr Thr Asp Glu  20  Ctg gag ctt gat gaa att Leu Glu Leu Asp Glu Ile  35  Caa ggt aat gta aag gca Gln Gly Asn Val Lys Ala  50  att gac gtc cct gcc aat Ile Asp Val Pro Ala Asn 65  70 gtt cga gga ctt cag gtc Val Arg Gly Leu Gln Val	101 149 197 245
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aag cgt gat ctg Lys Arg Asp Leu 10 gaa ttt gat gaa Glu Phe Asp Glu 25 aca tct gag aag Thr Ser Glu Lys 40 gca gga gcc tct Ala Gly Ala Ser 55 aga tat gat ctc Arg Tyr Asp Leu ttc aaa gaa agg Phe Lys Glu Arg 90 gga aaa atc cag Gly Lys Ile Gln 105 cct ttt gcg gta	ctc ttc c Leu Phe G cta tgt t Leu Cys P gaa ata a Glu Ile I gat gtt g Asp Val V 60 ctg tgt c Leu Cys L 75 ata aag g Ile Lys A aaa ttg a Lys Leu I gca gca g Ala Ala V	caa gcc ctg ggc Sin Ala Leu Gly 15 tt gaa ttt ggt Phe Glu Phe Gly 30 tta agt aaa gaa ile Ser Lys Glu 5 tt ctt tac aaa val Leu Tyr Lys ttg gaa gga ttg eu Glu Gly Leu 80 ct cca gtg tat la Pro Val Tyr 95 tt atc aca gaa ile Ile Thr Glu 110 ctc cgt aat	Met Pro Thr Val Ser Val  Cgc acc tac act gac gaa Arg Thr Tyr Thr Asp Glu 20 Ctg gag ctt gat gaa att Leu Glu Leu Asp Glu Ile 35 Caa ggt aat gta aag gca Gln Gly Asn Val Lys Ala 50 att gac gtc cct gcc aat Ile Asp Val Pro Ala Asn 65 70 gtt cga gga ctt cag gtc Val Arg Gly Leu Gln Val 85 aaa cgg gta atg cct gat Lys Arg Val Met Pro Asp 100 gag aca gct aag ata cgt Glu Thr Ala Lys Ile Arg	101 149 197 245 293

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Glu Lys Lys Cys Ala Val Val Arg Lys Ser Lys Gln Gly Arg Lys Arg
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ggc cca cac tgg tgt gaa tat tgt gcc aat ttc atg tgg ggg ctc atc
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403

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cag gag cta ttc ttg aag ttt gtg gat gaa aat tgg gaa ggt tcc ctc
Gln Glu Leu Phe Leu Lys Phe Val Asp Glu Asn Trp Glu Gly Ser Leu
5 10 15

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Lys Ser Lys Tyr Val Arg Gly Ser Asp Pro Val Leu Lys Leu Leu Asp

gac aat ggg aac att gct gaa gaa ctg agc att ctc aaa tgg aca cag
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Met Pro Lys Thr Met His Phe Leu Phe Arg Phe Ile Val Phe Phe Tyr
1 5 10 15

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Leu Trp Gly Leu Phe Thr Ala Gln Arg Gln Lys Lys Glu Glu Ser Thr

gaa gaa gtg aaa ata gaa gtt ttg cat cgt cca gaa aac tgc tct aag 201 Glu Glu Val Lys Ile Glu Val Leu His Arg Pro Glu Asn Cys Ser Lys 35 40 45

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96

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WO 99/53051	PCT/IB99/00712											
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tct agc aag ttg aag tca aac cag ctc ctt caa gaa gct ttg agc aga Ser Ser Lys Leu Lys Ser Asn Gln Leu Leu Gln Glu Ala Leu Ser Arg 5 10 15 20												
atg aag tgg gga gga ccc agc ttc cag ccc agg aag ccc act gta cct Met Lys Trp Gly Gly Pro Ser Phe Gln Pro Arg Lys Pro Thr Val Pro 25 30 35												
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157

205

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-10

ctg etc ett etc eta ecc eca gga tgg etg gac tgaetetgae ecagtteatg Leu Leu Leu Leu Pro Pro Gly Trp Leu Asp 40 gctactggtt ccgggcaggg aatgatataa gctggaaggc tccagtggcc acaaacaacc 318 378 cagettggge agtgeaggag gaaacteggg acegatteea metycyttgg ggaeceaeag accaaaaatt gcactctgag catcagagat gccagaatga gtgatgcggg gagatacttc 438 tttcgtatgg agaaaggaaa tataaaatgg aattataaat atgaccagct ctctgtgaac 498 gtgayageet tgacceacag geccaacats nktateeceg gtaccetgga gtetggetge 558 ttccagaatc tgacctgctc tgtgccctgg gcctgtgagc aggggacgcc ccctatgatc 618 626

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Cys Asp Leu Leu Gly Gln Phe Asn Leu Leu Gln Leu Asp Pro Asp Cys	
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Phe Gly Leu Arg Glu Phe Ser Gln Ile Arg Tyr Asp Ala Val Lys Ser	341
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-15

-10

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25

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gag gac gac ttc aac ta	-50 : qqc aqc aqc qtq	-45 gcc tcc gcc acc gtg cac	159
	Gly Ser Ser Val	Ala Ser Ala Thr Val His -30 -25	
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tat ccc ctt aac ctg ta		ttt acg ctg ttg gaa gct Phe Thr Leu Leu Glu Ala	<b>399</b>
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cca Pro -5	cct Pro	tgt Cys	cca Pro	ggg ggg	aag Lys 1	att Ile	gct Ala	tca Ser	aaa Lys 5	tta Leu	gcg Ala	ttt Phe	ttg Leu	cca Pro 10	cct Pro	309
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att Ile	Leu	aag Lys -55	gag Glu	gac Asp	gag Glu	Leu	ttg Leu -50	agt Ser	gag Glu	acc Thr	Gln (	caa Gln -45	gct Ala	gct Ala	ttt Phe	164

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415

415	
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atc ctg ctc acc gct ggc gct ggg ctg ctg gtg gtc caa gtt ctg aat ' Ile Leu Leu Thr Ala Gly Ala Gly Leu Leu Val Val Gln Val Leu Asn -5 1 5	308
ctg cag gcg cgg ctc cgg gtc ctg gag atg tat ttc ctc aat gac act Leu Gln Ala Arg Leu Arg Val Leu Glu Met Tyr Phe Leu Asn Asp Thr 10 15 20	356
ctg gcg gct gag gac agc ccg tcc ttc tcc ttg ctg cag tca gca cac Leu Ala Ala Glu Asp Ser Pro Ser Phe Ser Leu Leu Gln Ser Ala His 25 30 35	404
cct gga gaa cac ctg gct cag ggt gca tcg agg ctg cag tcc tgc agg Pro Gly Glu His Leu Ala Gln Gly Ala Ser Arg Leu Gln Ser Cys Arg 40 45 50 55	452
ccc aac tca cct ggg tcc gcg tca sca tgagcacttg ctgcagcggg Pro Asn Ser Pro Gly Ser Ala Ser Xaa 60	499
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ctc gac aag gca tcc atc att cga ctt aca att agc tat ctg aaa atg	245
Leu Asp Lys Ala Ser Ile Ile Arg Leu Thr Ile Ser Tyr Leu Lys Met 5 10 15	
agg gac ttt gct aac cag ggg gac cct ccg tgg aac ttg cga atg gaa Arg Asp Phe Ala Asn Gln Gly Asp Pro Pro Trp Asn Leu Arg Met Glu 20 25 30	293
ggc cct cca cct aac aca tca gta aaa gtt ata ggt gca cag cga agg Gly Pro Pro Pro Asn Thr Ser Val Lys Val Ile Gly Ala Gln Arg Arg 35 40 45	341
aga agc ccc agt gca cta gcc att gaa gta ttt gaa gca cat ttg gga Arg Ser Pro Ser Ala Leu Ala Ile Glu Val Phe Glu Ala His Leu Gly 50 55 60 65	389

WO 99/53051 PCT/IB99/00712 416 age cac att ttg cag tcc tgg atg gct ttg tat ttg cac taaatcagga 438 Ser His Ile Leu Gln Ser Trp Met Ala Leu Tyr Leu His aggaaaattt ttgtaca 455 <210> 783 <211> 453 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 85..168 <221> sig_peptide <222> 85..144 <223> Von Heijne matrix score 5 seq ALLSVCSTDVTTA/HA <221> misc feature <222> 284 <223> n=a, g, c or t <400> 783 ccccttgtgg ccaagcctgg aacatcacat ctgtacgttg caatctgtgg atcagctacg 60 agactgagag aaaggaatga aagg atg gaa gaa tta caa gat cag gca ctg 111 Met Glu Glu Leu Gln Asp Gln Ala Leu -20 -15 ctg tct gtc tgt tcc acg gat gta acc aca gca cac gcg tgg ctc acg 159 Leu Ser Val Cys Ser Thr Asp Val Thr Thr Ala His Ala Trp Leu Thr gta cta gtg tgataaatgc ttgttacatg aaggcgtgaa cagggatgag 208 aagagactto ctggagaaac aaaaggacta acaatcagga aggggaggtg atcggggcag 268 gagtaaagtg gacacntcag ctggtcccct gggtcgtcca cccgatgtcc cccattctcc 328 ccacttggcc tcccccacag gctctcggca aaggaccgtg ggaggcacct gtgacactgc 388 ccttttcctg tgcagctgtt tktcttcttc attctttca ctcctcgtta ctctttttt 448 tttca 453 <210> 784 <211> 587 <212> DNA <213> Homo sapiens <220> <221> CDS <222> 85..168 <221> sig_peptide <222> 85..144 <223> Von Heijne matrix score 5 seq ALLSVCSTDVTTA/HA <400> 784 ccccttgtgg ccaagectgg aacatcacat ctgtacgttg caatctgtgg atcagctacg 60 agactgagag aaaggaatga aagg atg gaa gaa tta caa gat cag gca ctg 111 Met Glu Glu Leu Gln Asp Gln Ala Leu -20 -15

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Leu Ser Val Cys Ser Thr Asp Val Thr Thr Ala His Ala Trp Leu Thr

159

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gagtaaagtg gacacctcag caaagccatt cgctgtgatc tctgattgtg cagtgtcatg
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tectgteace agagececet egtgtttgrk gttggecaat geegecagea tgatetagea
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ggccaaatcc taatctacca ttctctgaca ccagctggtc ccctgggtcg tccacccgat
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tetegtecaa aggagggggg tgetttetge tteageanga tecaceceae cetgggatee
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gagggagca atg gtg ggg cga gtg agg gtc tgc cgt aaa tat ccc ccg acc
                                                                    291
         Met Val Gly Arg Val Arg Val Cys Arg Lys Tyr Pro Pro Thr
                             -40
acc ctc tgg gaa ggt gct aga ggc cac agg caa att tca gtc tcc cca
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Thr Leu Trp Glu Gly Ala Arg Gly His Arg Gln Ile Ser Val Ser Pro
                       -25
                                           -20
387
Trp Asn Ile Cys Cys Ala Ala Ala Ala Ala Ala Ala Gly Ser Arg
-15
                   -10
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cgg ctg ggg acc cct cag caa atc gcc att gct cgc gag ggt gac ctc Arg Leu Gly Thr Pro Gln Gln Ile Ala Ile Ala Arg Glu Gly Asp Leu -30 -25 -20	154
ctg acc aag gag cgg ctg tgc tgt ggc ctg tcc atg ttc gag gtc atc Leu Thr Lys Glu Arg Leu Cys Cys Gly Leu Ser Met Phe Glu Val Ile -15 -10 -5	202
ctg acc cgc att cgg agc tac ctg cag gac ccc atc tgg cgg ggc cca Leu Thr Arg Ile Arg Ser Tyr Leu Gln Asp Pro Ile Trp Arg Gly Pro 1 5 10	250
ccg ccc acc aat ggc gtc atg cac gtc gat gag tgt gtg gag ttc cac Pro Pro Thr Asn Gly Val Met His Val Asp Glu Cys Val Glu Phe His 15 20 25 30	298
cgg ctg tgg agc gcc atg cag ttc gtg tac tgc atc cct gtg gga acc Arg Leu Trp Ser Ala Met Gln Phe Val Tyr Cys Ile Pro Val Gly Thr  35 40 45	346
aac gag ttc aca gct gag cag tgt ttc ggc gat ggc ttg aac tgg gct Asn Glu Phe Thr Ala Glu Gln Cys Phe Gly Asp Gly Leu Asn Trp Ala 50 55 60 ggt tck ccr kca ttg tcc tgc tsg gcc agc agc gtc gct ttg acc tgt	394
Gly Ser Pro Xaa Leu Ser Cys Xaa Ala Ser Ser Val Ala Leu Thr Cys 65 70 75 tcg act tct gtt acc acc tgc taaaagtgca gaggcaggac gggaag	442
Ser Thr Ser Val Thr Thr Cys  80  85	409
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tct atc ctg tgt aac tac aag gcc atc gaa atg ccc tca cac cag acc Ser Ile Leu Cys Asn Tyr Lys Ala Ile Glu Met Pro Ser His Gln Thr -50 -45 -40	153
tac gga ggg agc tgg aaa ttc ctg acg ttc att gat ctg gtt atc cag Tyr Gly Gly Ser Trp Lys Phe Leu Thr Phe Ile Asp Leu Val Ile Gln -35 -30 -25	201
gct gtc ttt ttt ggc atc tgt gtg ctg amt gat ctt tcc agt ctt ctg Ala Val Phe Phe Gly Ile Cys Val Leu Xaa Asp Leu Ser Ser Leu Leu -20 -15 -10	249

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Thr Arg Gly Ser Gly Asn Glu Glu Glu Arg Gln Leu Lys Lys Leu

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Ile Ser Leu Arg Asp Trp Met Leu Ala Val Leu Ala Phe Leu Leu Gly

15 20 25

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Phe Leu Leu

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His His Leu Gly Leu Pro Ala Ser Gln Pro Leu Pro Gly Ile Leu Ser

-65

-60

-55

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Ser Ser Pro Trp Gly Glu Ser Ser Ser Leu Leu Phe Pro Asp Cys

-30 -25 -20
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His Ile Ser Phe Pro Ala Leu Thr Gly Ser Gln Leu Leu Gly Asp Thr

296

-15 -10 -5
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Ile Pro Arg Pro His Leu Pro Pro Thr Ala Ala Cys

1 5 10 ,

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catcggcttg gcaaacggga gagaaaacag agcttcatgg gaaacagcgg caacagtggt 476
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			tcc					aag				ggt		ttt Phe		197
	cca					tta					ctg			ttt Phe		245
gat					gtg					ggt				ggc Gly 55	cca	293
				tat					cga						gat ' Asp	341
ttt Phe	taag	gtcg	cat a	attc	Ė.			65					70			359
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	-50					-45					-40	_		Glu aac		213
Gly -35	Leu	Thr	Ala	Gln	Val -30	Leu	Asp	Ala	Ser	Ser -25	Leu	Ser	Phe	Asn	Thr -20	213
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														ctt Leu		309
gca Ala			tat						_				-	cat His	_	357

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                                       -85
                                                           -80
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                                                                       98
Arg Val Ser Ala Cys Arg Gly Gly Thr Pro Gly Gly Gly Arg Gly Gln
            -75
                                -70
age cae tgc aga gga cca gae tgg gaa aac aac gat atg gca gga gee
                                                                      146
Ser His Cys Arg Gly Pro Asp Trp Glu Asn Asn Asp Met Ala Gly Ala
        -60
                            ~55
                                                -50
agt ctt ggg gcc cgc ttc tac cgg cag atc aaa aga cat ccg ggg atc
                                                                      194
Ser Leu Gly Ala Arg Phe Tyr Arg Gln Ile Lys Arg His Pro Gly Ile
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                                             -35
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Ile Pro Met Ile Gly Leu Ile Cys Leu Gly Met Gly Ser Ala Ala Leu
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Lys Glu Gln Pro Gly Ala Leu Glu Pro Pro Glu Pro Gln
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gag cag ctg gcc aaa tac ctt caa ctg aga aat gtc att gag cga ctc Glu Gln Leu Ala Lys Tyr Leu Gln Leu Arg Asn Val Ile Glu Arg Leu 45 50 55	254
Cag gaa gct aag cac tcg gag tta tat atg cag gtg gat ttg ggc tgt Gln Glu Ala Lys His Ser Glu Leu Tyr Met Gln Val Asp Leu Gly Cys 60 70 75	302
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gcc ctg gga tat ggt ttt ttc ctg gag ttg aca ctg gca gaa gct ctc Ala Leu Gly Tyr Gly Phe Phe Leu Glu Leu Thr Leu Ala Glu Ala Leu 95 100 105	398
aag ttc att gat cgt aag agc tct ctc ctc aca gag ctc agc aac agc Lys Phe Ile Asp Arg Lys Ser Ser Leu Leu Thr Glu Leu Ser Asn Ser 110 115 120	446
ctc acc aag gac tcc atg aat atc aaa gcc cat atc cac atg ttg cta Leu Thr Lys Asp Ser Met Asn Ile Lys Ala His Ile His Met Leu Leu 125 130 135	494
gag ggg ctt aga gaa cta caa ggc ctg cag aat ttc cca gag aag cct Glu Gly Leu Arg Glu Leu Gln Gly Leu Gln Asn Phe Pro Glu Lys Pro 140 150 155	542
Cac cat tgacttette c His His	559
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agt gcc atg ggc ttc act gcg gcg gga atc gcc tcg tcc tcc ata gca Ser Ala Met Gly Phe Thr Ala Ala Gly Ile Ala Ser Ser Ser Ile Ala	313

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tcg ggc ago Ser Gly Ser	ctt gtg g Leu Val 1 85	gct act ctg Ala Thr Leu	cag tca ct Gln Ser Le	g gga gca a u Gly Ala T	ict qqa ctc	409
tcc gga ttg Ser Gly Leu	acc aag to Thr Lys 1	tkc atċ ctg Xaa Ile Leu	ggc tcc at	e Gly Ser A	cc att qcq	457
gct gtc att Ala Val Ile 115	Ala Arg 1	ttc tac tag Phe Tyr	ctccctg ccc			508
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aag gct tcc Lys Ala Ser 25	Trp Arg A	agg gaa caa Arg Glu Gln 10	tgg cat gg Trp His Gl	a cct tgđ đ y Pro Xaa X	ga gtc aga aa Val Arg 40	209
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cat tct ata His Ser Ile	gtg ctt g Val Leu A 60	cc gtg act la Val Thr	cag gcg cae Gln Ala Hi: 65	c agt gca a s Ser Ala L 7	ys Gly Ser	305
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Met Val Gly Val Ser Val Cys 1 5	
cat cac att cga gtg ggg att aag aga agg aag gct gcc ttg ctg gag His His Ile Arg Val Gly Ile Lys Arg Arg Lys Ala Ala Leu Leu Glu 10 15 20	220
ctg tgt ggt ctt ctc caa gtg aga gtc gca ggc aat aga act act ttg Leu Cys Gly Leu Leu Gln Val Arg Val Ala Gly Asn Arg Thr Thr Leu 25 30 35	268
ctt ttg gag gaa aag mgg aat tca ttt tca gca nnc acr aga aaa gca Leu Leu Glu Glu Lys Arg Asn Ser Phe Ser Ala Xaa Thr Arg Lys Ala 40 45 50 55	316
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Met Pro Ser Arg Thr Ala 1 5	
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gat cgc agc gtg cgt ttc cct aat gat gtc ctg ttc ttg gac cac atc Asp Arg Ser Val Arg Phe Pro Asn Asp Val Leu Phe Leu Asp His Ile 25 30 35	211
cgg cag ggt gac ctg gag cag gtg ggg cgc ttc atc cgg act cgg aaa Arg Gln Gly Asp Leu Glu Gln Val Gly Arg Phe Ile Arg Thr Arg Lys 40 45 50	259
gtc tcc ctg gcc acc atc cac ccc tca ggc ctg gcc gcc ttg cat gaa Val Ser Leu Ala Thr Ile His Pro Ser Gly Leu Ala Ala Leu His Glu 55 60 65 70	307
gcc gtg ctc tct gga aac ctg gaa tgc gtg aag ctg ctg gtc aaa tac Ala Val Leu Ser Gly Asn Leu Glu Cys Val Lys Leu Leu Val Lys Tyr 75 80 85	355
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Ile Arg Gln Asp His Ile

WO 99/53051 PCT/IB99/00712

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Gln Leu Asp Asp Glu Glu Met Tyr Ser Ala His Met Pro Ala His Leu
Arg Cys Asp Ala Cys Arg Ala Val Ala Tyr Gln Val Ser Pro Ser Pro
Leu Ser Pro Ala Leu Leu Thr Pro Leu Leu Lys Pro Ala Pro Thr Gly
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Leu Arg Gly Ala Arg Cys Gly Val Gln Met Thr Gln Phe Pro Leu Ser
                       . 1
Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Thr Ser
               15
                                    20
His Ile Ile Asn Ile Phe Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys
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Ala Pro Trp
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      .-5
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 Pro Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln
Ser Ile Gly Ser Tyr Leu Asn Trp Tyr Gln His Lys Pro Gly His Ala
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Pro Arg Leu Leu Ile Tyr Ala Ala Thr Thr Leu Ser Arg Gly Gly Pro
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Ala Arg Phe Ser
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                        -10
                                            -5
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Arg Lys Lys Lys Asp Ile Arg Asp Tyr Asn Asp Ala Asp Met Ala
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Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asn Phe
Ser Thr Tyr Glu Met His Trp Ile Arg Gln Ala Pro Gly Lys Gly Pro
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Glu Trp Val Xaa Tyr Val Ser Gly Gly Gly Gly Thr Xaa Xaa Asn Ala
Xaa Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Asn Ser
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Phe Val Tyr Leu Gln Met Asp Ser Leu Arg Val Glu Asp Thr Ala Leu
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Pro Gly Thr Ser Leu Thr Leu Ser Cys Ala Gly Ser Gly Phe Ser Phe
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Ser Asp Tyr Gly Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu
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Glu Trp Val Ala Val Ile Ser His Asp Gly Asn Asn Lys Tyr Tyr Gly
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                                    55
Gly Ser Met Lys Gly Arg Val Thr Ile Ser Arg Asp Asn Ser Arg His
Thr Val Ser Leu Gln Met Ser Ser Leu Gly Pro Glu Asp Thr Ala Val
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Tyr Tyr Cys Ala Lys Asp Arg Thr Gly Gly
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                                   -10
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           7
Pro Ser Gly Thr Leu Ser Leu Thr Cys Thr Val Xaa Gly Xaa Xaa Ile
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                                            25
Thr Asn Tyr Tyr Trp Ser Xaa Ile Arg Gln Ser Pro Gly Lys Gly Leu
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Val Glu Leu Ser Ile His Trp Val Arg Gln Ser Pro Gly Lys Gly Leu

437 Glu Trp Met Gly Gly Phe Asp Leu Glu Ser Gly Glu Thr Ile Tyr Ala Gln Arg Phe Gln Gly Arg Ile Thr Met Thr Glu Asp Ser Ser Ser Asp Thr Ala Phe Met Glu Leu Ile Ser Leu Arg Pro Glu Asp Ala Ala Val Tyr Tyr Cys Ala Thr Ile Arg Leu Pro Val Val Leu Phe Phe Ala Ala 100 105 Ser Gly Ala Arg Glu Pro Trp Ser Pro Ser Pro Gln Xaa Pro Arg 115 120 <210> 825 <211> 37 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -18..-1 <400> 825 Met Trp Leu Pro Leu Val Leu Leu Leu Ala Val Leu Leu Leu Ala Val -15、 -10 Leu Cys Lys Val Tyr Leu Gly Leu Phe Ser Gly Ser Ser Pro Asn Pro 1 Phe Ser Glu Glu Arg 15 <210> 826 <211> 51 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -25..-1 <400> 826 Met Glu Leu Ala Leu Arg Arg Ser Pro Val Pro Arg Trp Leu Leu Leu -20 -15 . Leu Pro Leu Leu Gly Leu Asn Ala Gly Ala Val Ile Asp Trp Pro -5 1 Thr Glu Glu Gly Lys Glu Val Trp Asp Tyr Val Thr Val Arg Lys Asp 10 15 Ala Tyr Met 25 <210> 827 <211> 131 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -19..-1 <400> 827 Met Ala Trp Thr Pro Leu Phe Leu Phe Leu Leu Thr Cys Cys Pro Gly -15 -10 Ser Asn Ser Gln Ala Val Xaa Thr Gln Glu Pro Leu Thr Asp Cys Val Pro Arg Xaa Thr Val Thr Leu Thr Cys Gly Ser Ser Ile Gly Ala Val

15

*31.00 02 1* 

Thr Asn Gly His Phe Pro Tyr Trp Phe Gln Gln Lys Pro Gly Gln Ala 30 40 45

Pro Arg Thr Leu Ile Ser Asp Thr Phe Asn Arg Gln Ser Ser Thr Pro

Ala Arg Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Val Leu Thr Leu
65 70 75

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Leu Ser Gln

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Ser Cys Leu Ser Leu Pro Ser Gly Trp Asp Cys Arg Arg Pro Pro Pro 30 35 40

Arg Leu Ala Asn Ser Cys Val Phe Gly Gly Asp Gly Val Ser Pro

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Gly Ala Ala Glu Thr Lys Pro His Pro Ala Glu Gly Gln Trp Arg Ala

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439
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440

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Thr Lys Asp Ser Arg Pro Lys Leu Pro Gln Thr Leu Ser Arg Gly Trp
15 20 25

Gly Asp Gln Leu Ile Trp Thr Gln Thr Tyr Glu Glu Ala Leu Tyr Lys 30 35 40

Ser Lys Thr Ser Asn Lys Pro Leu Met Ile Ile His His Leu Asp Glu 45 50 55 60

Cys Pro His Ser Gln Ala Leu Lys Lys Val Phe Ala Glu Asn Lys Glu 65 70 75

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Met Arg Pro Gly Leu Ser Phe Leu Leu Ala Leu Leu Phe Phe Leu Gly -20 -15 -10 -5

Gln Ala Ala Gly Asp Leu Gly Asp Val Gly Pro Pro Ile Pro Ser Pro

Gly Phe Ser Ser Phe Pro Gly Val Asp Ser Ser Ser Ser Phe Ser Ser 15 20 25

Ser Ser Arg Ser Gly Ser Ser Ser Ser Arg Ser Leu Gly Ser Gly Gly 30 35 40

Ser Val Ser Gln Leu Phe Ser Asn Phe Thr Gly Ser Val Asp Asp Arg
45 55 60

Gly Thr Cys Gln Cys Ser Val Ser Leu Pro Asp Thr Thr Phe Pro Val
65 70 75

Asp Arg Val Glu Arg Leu Glu Phe Thr Ala His Val Leu Ser Gln Lys 80 85 90

Phe Glu Lys Glu Leu Ser Lys

<210> 835

<211> 147 <212> PRT

<213> Homo sapiens

<220>

<221> SIGNAL

<222> -26..-1

<400> 835

Met Asp Leu Leu His Lys Asn Met Lys His Leu Trp Phe Phe Leu Leu -25 -20 -15

Leu Val Ala Ala Pro Arg Trp Val Arg Ser Gln Val Gln Leu Xaa Glu

Ser Gly Pro Gly Leu Val Lys Pro Ser Gly Thr Leu Ser Leu Ile Cys

WO 99/53051 441 Gly Val Ser Gly Asp Ser Val Thr Ile Ser Gly Trp Trp Ser Trp Val 30 Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile Ser Glu Ile Asp His 45 Gly Gly Asn Thr Asn Tyr Asn Pro Ser Leu Lys Ser Arg Val Xaa Ile 60 Ser Leu Asp Lys Ser Lys Asn Lys Phe Ser Leu Arg Leu Thr Ser Val 80 Thr Ala Ala Asp Thr Ala Met Tyr Xaa Cys Ala Arg Gly Gly Ala Xaa 95 Ser Ser Ser Ala Phe Asp Val Trp Gly Leu Xaa Thr Met Val Ile Ile 105 Ser Ser Ala 120 <210> 836 <211> 139 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -19..-1 <400> 836 Met Asp Ile Leu Cys Ser Thr Leu Leu Leu Thr Val Pro Ser Trp -15 -10 Val Leu Ser Gln Val Thr Leu Xaa Glu Ser Gly Pro Ala Leu Val Lys Ala Thr Gln Thr Leu Arg Leu Thr Cys Thr Phe Ser Gly Phe Ser Leu Ser Thr Asn Arg Met Arg Val Ser Trp Ile Arg Gln Pro Pro Gly Lys 40 Ala Leu Glu Trp Leu Ala Arg Ile Asp Trp Asp Asp Tyr Lys Arg Tyr 55 Ser Thr Ser Leu Lys Thr Arg Val Thr Ile Ser Lys Asp Thr Ser Lys 70 Asn Gln Val Ile Leu Thr Met Thr Asn Val Asp Pro Ala Asp Thr Ala 85 Thr Tyr Tyr Cys Ala Arg Leu Ser Thr Ala Ala Thr Pro Gln Phe Phe 100 Asp Phe Trp Gly Gln Gly Val Leu Val Ser Val 115 <210> 837 <211> 139 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -19..-1 Met Xaa His Leu Trp Phe Phe Leu Leu Leu Val Ala Ala Pro Arg Trp -15 -10 Val Leu Ser Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Xaa Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Asp Ser Ile

Ser Ser Tyr Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu

Glu Trp Ile Gly Tyr Ile Tyr Tyr Ser Gly Ser Thr Asn Tyr Asn Pro 55 Ser Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr 85 Tyr Cys Ala Arg Xaa Leu Xaa Tyr Tyr Asp Arg Ser Gly Tyr Phe Arg 100 Tyr Phe Asp Tyr Trp Gly Gln Gly Thr Trp Ser 115 <210> 838 <211> 136 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -19..-1 <400> 838 Met Lys His Leu Trp Phe Phe Leu Leu Leu Val Ala Ala Pro Arg Trp -15 -10 Val Leu Ser Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Asp Ser Gly Asn Tyr Tyr Trp Ser Trp Ile Arg Gln Pro Ala Gly Lys 35 40 Gly Leu Glu Trp Ile Gly Arg Ile Tyr Ser Thr Gly Ser Thr Asn Tyr 55 Asn Pro Ser Leu Ser Ser Arg Val Gln Ile Ser Leu Asp Thr Ser Lys 70 Asn Leu Leu Ser Leu Asn Leu Thr Ser Val Thr Ala Ala Asp Thr Ala 85 Val Tyr Phe Cys Ala Arg Thr Phe Pro Phe Tyr Trp Tyr Leu Asp Leu 100 Trp Gly Arg Gly Ile Leu Val Thr <210> 839 <211> 143 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -19..-1 <400> 839 Met Lys His Leu Trp Phe Phe Leu Leu Val Ala Ala Pro Arg Trp -10 Val Leu Ser Gln Val Gln Leu Gln Glu Ser Gly Pro Arg Leu Val Lys Pro Ser Gln Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Gly Gly Tyr Phe Trp Ser Trp Ile Arg Gln His Pro Gly Arg Gly Leu Glu Trp Ile Gly Tyr Ile Tyr Tyr Asn Trp Ser Thr Tyr Tyr 55 Asn Pro Ser Leu Arg Ser Arg Val Thr Met Ser Met Asp Thr Ser Lys

Asn Gln Phe Ser Leu Asn Leu Asn Ser Val Thr Ala Ala Asp Thr Xaa

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85
                                                 90
Met Tyr Tyr Cys Ala Arg Gly Arg Gly Arg Leu Gly Trp Phe Xaa Xaa
                       100
                                             105
Xaa Gly Xaa Gly Xaa Pro Gly His Arg Leu Ile Ser Arg Pro Gly
                    115
<210> 840
<211> 111
<212> PRT
<213> Homo sapiens
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<221> SIGNAL
<222> -19..-1
<400> 840
Met Lys His Leu Trp Phe Phe Leu Leu Leu Val Ala Ala Pro Arg Trp
                -15
                                     -10
Val Leu Ser Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys
Pro Ser Glu Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile
Arg Thr Gly Ser Tyr Tyr Trp Thr Trp Val Arg Gln Pro Pro Gly Lys
                                         40
Gly Leu Glu Trp Ile Gly Tyr Ile Tyr Tyr Thr Gly Asp Thr Tyr Tyr
Asn Pro Ser Leu Lys Ser Arg Ile Thr Met Ser Leu Asp Thr Xaa Xaa
Asn Gln Phe Xaa Leu Ser Leu Thr Ser Val Thr Val Ala Asp Thr
                            85
<210> 841
<211> 53
<212> PRT
<213> Homo sapiens
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<221> SIGNAL
<222> -15..-1
<400> 841
Met Lys Leu Ser Val Cys Leu Leu Leu Val Thr Leu Ala Leu Cys Cys
                    -10
Tyr Gln Ala Asn Ala Glu Phe Cys Pro Ala Leu Val Ser Glu Leu Leu
                                10
Asp Phe Phe Phe Ile Ser Glu Pro Leu Phe Lys Leu Ser Leu Ala Lys
       20
Phe Asp Ala Pro Arg
 . 35
<210> 842 -
<211> 23
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -16..-1
<400> 842
Met Ser Pro Val Leu Leu Val Leu Ser Leu Ser Gln Cys Leu Leu Ser
                       -10
Asp Pro Val Ile Pro Gly Leu
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<210> 843
<211> 93
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -19..-1
<400> 843
Met Lys His Leu Trp Phe Phe Leu Leu Leu Val Ala Ala Pro Arg Trp
            -15
                                   -10
Val Leu Ser Gln Val Arg Leu Gln Glu Ser Gly Pro Arg Leu Val Lys
Pro Ser Glu Xaa Leu Ser Leu Thr Cys Ser Val Ser Gly Val Ser Val
Thr Asn Phe Phe Trp Asn Trp Ile Arg Lys Pro Pro Gly Lys Gly Leu
Glu Trp Leu Gly Tyr Met Ser Tyr Gly Val Ser Thr Asn Tyr His Pro
Ala Tyr Gln Ser Arg Val Ser Ile Ser Ile Asp Thr Trp
<210> 844
<211> 139
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -19..-1
<400> 844
Met Lys His Leu Trp Phe Phe Leu Leu Val Ala Ala Pro Arg Trp
               -15
                                    -10
Val Leu Ser Gln Val Gln Leu Gln Glu Ala Gly Pro Arg Leu Val Lys
Pro Ser Glu Ala Leu Ser Leu Thr Cys Thr Val Ser Gly Val Ser Ser
Ser Asn Tyr Asp Trp Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu
                   35
Glu Trp Ile Gly Tyr Ile Asp Asp Ser Lys Asn Arg Gly Ser Thr Thr
Tyr Asn Pro Ser Leu Lys Ser Arg Val Thr Ile Ser Xaa Asp Thr Ser
Lys Xaa Gln Leu Ser Leu Arg Leu Thr Ser Val Thr Xaa Ala Asp Thr
Ala Val Tyr Tyr Cys Ala Arg Lys Ser Ser Met His Ser Ser Gly Trp
                       100
His Asn Arg Ser Leu Tyr Trp Tyr Phe Asp Pro
                    115
<210> 845
<211> 134
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -26..-1
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<400> 845
Met Asp Leu Leu His Lys Asn Met Lys Asp Leu Trp Phe Phe Leu Leu
                        -20
Leu Val Ala Ala Pro Arg Trp Val Leu Ser Gln Val Leu Gln Glu Ser
                    -5
Gly Pro Gly Leu Val Lys Pro Ser Gly Thr Leu Ser Leu Thr Cys Ala
                                15
Val Ser Gly Gly Ser Ile Ile Ser Ser Asn Trp Trp Ser Trp Val Arg
                            30
Gln Thr Pro Gly Lys Gly Leu Glu Trp Ile Gly Glu Ile Tyr Glu Asp
                        45
Gly Ile Thr Asn Tyr Asn Pro Ser Leu Lys Ser Arg Val Ile Ile Ser
Val Asp Lys Ala Lys Asn Gln Phe Ser Leu Lys Met Arg Ser Val Thr
                                    80
Ala Ser Asp Thr Ala Val Tyr Tyr Cys Ala Arg Gly Ser Ser Ser Val
                                95
           90
Arg Thr Asp Tyr Trp Gly
        105
<210> 846
<211> 144
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -19..-1
<400> 846
Met Lys His Leu Trp Phe Phe Leu Leu Leu Val Ala Ala Pro Arg Trp
                -15
                                    -10
Val Leu Ser Gln Val Gln Leu Gln Glu Ser Gly Ser Gly Pro Val Asp
Xaa Xaa Gln Thr Leu Xaa Leu Thr Cys Thr Xaa Ser Gly Val Ser Ile
                        20
Ser Ser Ser Asp Asn Cys Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys
Gly Leu Glu Trp Ile Gly Tyr Ile Tyr His Ser Gly Gly Thr Tyr Tyr
                                    55
Asn Pro Thr Leu Lys Ser Arg Val Thr Ile Ser Xaa Asp Arg Ile Arg
Asn Gln Phe Ser Leu Lys Leu Ser Ser Val Thr Ala Xaa Asp Thr Ala
                            85
Val Tyr Xaa Cys Gly Arg Ala Gln Gly Arg Met Gly Ile Gly Thr Thr
                        100
                                            105
Ile Phe Asp Leu Trp Gly Gly Gly Gln Trp Ser Pro Ser Leu Gln Pro
                    115
<210> 847
<211> 140
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -19..-1
<400> 847
Met Asp Trp Thr Trp Arg Ile Leu Phe Leu Val Ala Ala Ala Thr Gly
               -15
                                    -10
Ala His Ser Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys
```

446 Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Xaa Phe . 20 Thr Xaa Xaa Ala Xaa His Trp Val Arg Gln Ala Pro Gly Gln Arg Leu Glu Trp Met Gly Trp Ile Asn Ala Ala Xaa Gly Xaa Thr Xaa Tyr Ser Gln Xaa Phe Gln Xaa Arg Val Thr Xaa Thr Arg Asp Thr Ser Ala Ser Thr Val Ser Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Phe Cys Ala Arg Asp Trp Glu Ile Ala Val Val Pro Thr Ala Ile 100 105 Asn Ser Tyr Gly Phe Asp Pro Gly Ala Arg Glu Pro <210> 848 <211> 52 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -26..-1 <400> 848 Met Glu Ala Arg Val Glu Arg Ala Val Gln Lys Arg Gln Val Leu Phe -20 Leu Cys Val Phe Leu Gly Met Ser Trp Ala Gly Ala Glu Pro Leu Arg -5 Tyr Phe Val Ala Glu Glu Thr Glu Arg Gly Thr Xaa Leu Thr Asn Leu Ala Lys Asp Leu 25 <210> 849 <211> 134 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -19..-1 <400> .849 Met Asp Trp Thr Trp Ser Ile Leu Phe Leu Val Ala Ala Ala Thr Gly -15 . -10 Ala His Ser Gln Val Gln Leu Val Gln Ser Gly Gly Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe 20 Thr Arg Tyr Asp Ile Asn Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met Gly Trp Ile Ser Ala Xaa Asn Gly Asn Thr Asn Tyr Ala 55 Gln Xaa Val Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Arg 70 Thr Ala Tyr Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Ile 85 Tyr Tyr Cys Ala Arg Glu Ile Xaa Val Xaa Xaa Cys Asp Gly Gln Leu 100 Gly Pro Gly Asn Leu Val 110

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<210> 850
<211> 140
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -26..-1
<400> 850
Met Asp Val Leu His Lys His Met Lys His Leu Trp Phe Phe Leu Leu
                        -20
                                             -15
Leu Val Ala Ala Pro Arg Trp Val Leu Ser Gln Glu Gln Leu Arg Gln
                    -5
Trp Gly Ala Xaa Leu Leu Lys Pro Ser Glu Thr Leu Ser Leu Thr Cys
Ser Val Tyr Gly Gly Ser Phe Asn Gly Tyr Tyr Trp Ser Trp Ile Arg
Gln Ser Pro Gly Lys Gly Leu Glu Trp Ile Gly Gly Ile Asn His Ser
                        45
Gly Ser Thr Leu Ser Asn Pro Ser Leu Lys Ser Arg Val Asp Leu Ser
                                         65
Val Asp Ala Ser Lys Asp Gln Val Ser Leu Arg Leu Lys Leu Val Thr
                75
Ala Ala Asp Thr Ala Val Tyr Phe Cys Ala Arg Pro His Tyr Asp Met
                                95
Ser Thr Asp Ser Ser Phe Asp Gly Phe Asp Leu Trp
                            110
<210> 851
<211> 44
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -15..-1
<400> 851
Met Met Leu Leu Ala Leu Phe Phe Leu Leu Arg Ile Ala Leu Ala Ser
Gln Gly Leu Leu Trp Phe His Thr Asn Phe Lys Val Phe Val Val Ser
Ile Cys Val Lys Thr Ile Ile Gly Ile Ser Gly Gly
        20
                            25
<210> 852
<211> 78
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -19..-1
<400> 852
Met Asp Trp Thr Trp Arg Ile Leu Phe Leu Val Ala Ala Ala Thr Gly
                                     -10
                -15
Ala Leu Ser Gln Val Gln Leu Val Gln Ser Gly Gly Glu Val Lys Lys
Pro Gly Ala Ser Val Arg Val Ser Cys Lys Ala Ser Gly Tyr Ser Phe
```

Ile Gly Tyr Tyr Val His Trp Ile Arg Gln Thr Pro Gly Arg Xaa Leu

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30 '
                    35
                                         40
                                                             45
Glu Trp Met Gly Trp Val Asn Pro Xaa Thr Gly Asp Asn Gly
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<210> 853
<211> 44
<212> PRT
<213> Homo sapiens
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<221> SIGNAL
<222> -37..-1
<400> 853
Met Phe Phe Gln Phe Trp Lys Ser Ser Ala Tyr Leu Ile Phe Val Ser
        -35
                            -30
Ile Cys Lys Gly Phe Leu Pro Val Tyr Leu Leu Leu Val Leu Ser Leu
                        -15
Ser Leu Ser Leu Cys Cys Ser Leu Leu Ser Leu
<210> 854
<211> 128
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -19..-1
<400> 854
Met Asp Trp Thr Trp Arg Ile Leu Phe Leu Val Ala Ala Ala Thr Gly
                -15
                                    -10
Val His Ser Gln Val His Leu Val Gln Ser Gly Ala Glu Val Lys Lys
Pro Gly Thr Pro Val Asn Ile Ser Cys Lys Ala Phe Gly Tyr Thr Phe
                        20
Pro Ala Phe Ala Ile His Trp Val Arg Gln Ala Pro Gly Gln Ser Leu
                    35
                                        40
Glu Trp Met Gly Trp Val Asn Ile Gly His Gly Asn Thr Lys Tyr Ser
                50
                                    55
Gln Lys Phe Gln Gly Arg Leu Ala Ile Ser Arg Asp Thr Ser Ala Asn
                                70
Ile Val Tyr Xaa Glu Leu Ser Gly Leu Arg Ser Glu Asp Thr Ala Val
                            85
Tyr Tyr Cys Ala Arg Asp Asn Leu Phe Phe Gly Ser Met Gly Phe Asp
<210> 855
<211> 152
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -16..-1
<400> 855
Met Ala Trp Thr Val Leu Leu Gly Leu Leu Ser His Cys Thr Gly
                        -10
Ser Val Thr Ser Tyr Val Leu Thr Gln Pro Pro Ser Val Ser Val Ala
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Pro Gly Lys Thr Ala Ser Ile Thr Cys Gly Gly Asp Asn Ile Glu Ser

449 20 25 30 Gln Val Val His Trp His Gln Gln Lys Pro Gly Gln Ala Pro Ile Leu 40 Val Ile Tyr Asp Asp Thr Asp Arg Pro Ser Gly Ile Pro Asp Arg Phe 55 Ser Gly Ser Asn Ser Gly His Thr Ala Thr Leu Thr Ile Ser Arg Val 70 75 Glu Ala Gly Asp Glu Ala Asp Tyr Tyr Cys Gln Val Trp Asp Arg Ser 85 90 Ser Gly Gln Gly Ile Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Arg 105 Gln Pro Lys Ala Ala Pro Ser Val Thr Leu Phe Pro Pro Ser Ser Glu 120 Glu Leu Gln Ala Asn Lys Ala Thr 130 <210> 856 <211> 48 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -15..-1 <400> 856 Met Arg Leu Leu Phe Leu Leu Phe Val Cys Phe Ser Arg Gln Gly -10 -5 Leu Ala Leu Ser Leu Arg Leu Glu Cys Ser Gly Met Ile Met Ala Tyr 10 Cys Ser Ile Ser Leu Pro Gly Ser Ser Ser Pro Leu Thr Ser Ala Ser 25 <210> 857 <211> 74 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -19..-1 <400> 857 Met Lys His Leu Trp Phe Phe Leu Leu Val Ser Ala Pro Arg Trp ~15 -10 Val Leu Ser Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gly Arg Leu Ser Leu Ala Cys Asp Val Val Glu Leu Ser Pro 25 Pro Ala Pro Arg Gly Gly Ser Ala Val His Leu Arg Asn Leu Ser Ser 35 Trp Glu Pro His Leu Gln Pro Val Ser Gly 50 <210> 858 <211> 57 <212> PRT

<213> Homo sapiens

<220>

<221> SIGNAL

<222> -32..-1

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<400> 858
Met Thr Tyr Phe Pro Leu Gly Arg Tyr Pro Val Met Gly Leu Leu Asp
                           -25
       -30
                                               -20
Gln Met Val Val Phe Leu Leu Leu Val Ser Thr Leu Ser Ser
                       -10
                                           - 5
Val Val Leu Leu Val Cys Ile Pro Thr Ser Ser Val Lys Leu Phe
                               10
Pro Phe His His Ile His Thr Asn Trp
           20
<210> 859
<211> 30
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -19..-1
<400> 859
Met Glu Phe Gly Leu Ser Trp Val Leu Leu Val Ala Met Leu Arg Gly
             -15
                                   -10
Leu Gln Cys Gln Val Gln Leu Val Glu Ser Gly Gly Thr Ala
<210> 860
<211> 57
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -15..-1
<400> 860
Met Tyr Leu Ser Leu Leu Ile Leu Leu Glu Asn Val Ser Gly Phe
                   -10
Pro Phe Pro Leu Ile Phe Gln Leu His Ala Ser Pro Gly His Lys Ile
                               10
Leu Pro Asp Cys Met Ile Tyr Ser Ile Thr Val Ser Leu Met Phe Pro
                           25
Val Val Asp Tyr Ile Ser Thr Gln Gly
   35
<210> 861
<211> 31
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -28..-1
<400> 861
Met Met Arg Ala Phe Tyr Leu Ala Ile Leu Phe Cys Leu Ser Leu Ser
         -25 ·
                               -20
Leu Trp Phe Xaa Cys Leu Leu Phe Leu Leu Phe Ala Trp Pro Gly
      -10
                           -5
<210> 862
<211> 102
<212> PRT
<213> Homo sapiens
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<220>
<221> SIGNAL
<222> -20..-1
<400> 862
Met Ala Trp Thr Pro Leu Leu Phe Leu Thr Leu Leu His Cys Thr '
                   -15
                                        -10
Gly Ser Leu Ala Gln Leu Val Leu Thr Gln Ser Pro Ser Ala Ser Ala
Ser Leu Gly Ala Ser Val Lys Leu Thr Cys Thr Leu Ser Ser Gly His
                            20
Ser Asn Tyr Gly Ile Ala Trp Tyr Gln Gln Pro Glu Lys Gly Pro
                        35
Arg Phe Leu Met Lys Val Asn Ser Asp Gly Ser His Met Lys Ala Asp
                    50
Gly Ile Pro Asp Arg Phe Ser Gly Ser Ser Ser Gly Ala Glu Arg Tyr
Leu Ser Ile Ser Ser Leu
            80
<210> 863
<211> 18
 <212> PRT
<213> Homo sapiens
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<221> SIGNAL
<222> -14..-1
Met Pro Leu Ala Leu Phe Phe Leu Leu Ser Val Ala Leu Ala Ile Gln
                -10
Gly Gln
<210> 864
<211> 129
<212> PRT
<213> Homo sapiens
. <220>
<221> SIGNAL
<222> -19..-1
<400> 864
Met Asp Trp Thr Trp Arg Xaa Phe Cys Leu Leu Ala Val Ala Pro Gly
                -15
                                    -10
Ala His Ser Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys
Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe
                      · 20
Thr Ser His Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu
                    35
                                        40
Glu Trp Met Gly Ile Ile Tyr Pro Asp Ser Asp Thr Thr Lys Tyr Xaa
                50
                                    55
Gln Asn Phe Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Ser
                                70
Thr Val Tyr Met Glu Leu Ser Ser Leu Thr Ser Asp Asp Thr Ala Val
                            85
                                                90
Tyr Tyr Cys Ala Arg Glu Ala Tyr Ser Gly Ser Tyr Arg Phe Asp Tyr
                        100
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Trp 110

<212> PRT

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<210> 865
<211> 124
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -26..-1
<400>.865
Met Asp Leu Met Cys Lys Lys Met Arg His Leu Trp Phe Leu Leu
                        -20
Leu Val Ala Ala Pro Arg Trp Val Leu Ser Gln Leu Gln Leu Gln Glu
Ser Gly Pro Gly Leu Val Lys Ala Ser Glu Thr Leu Ser Leu Ala Cys
                               15
Ser Val Ser Gly Asp Ser Ile Ser Ser Gly Asn Tyr Tyr Trp Gly Trp
Ile Arg Gln Pro Pro Gly Lys Gly Leu Gln Trp Leu Gly Ser Leu Trp
                        45
Asn Arg Gly Gly Pro Gln Tyr Asn Xaa Ser Leu Lys Asn Arg Val Thr
                   60
Val Ser Val Asp Thr Ser Thr Asn His Phe Phe Leu Arg Leu Asn Ser
               75
Val Asn Xaa Gly His Gly Asn Leu Leu Cys Ala
<210> 866
<211> 32
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -16..-1
<400> 866
Met Arg Xaa Xaa Leu Xaa Leu Ser Val Leu Leu Gly Xaa Xaa Xaa
 -15
                    -10
Lys Xaa Asp Phe Val Gly His Gln Val Leu Arg Ile Ser Val Ala Asp
<210> 867
<211> 38
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -36..-1
<400> 867
Met Ala Glu Ser Arg Glu Glu Gly Glu Ser Cys Val Glu Ser His Cys
                       -30
                                            -25
Val Leu Phe Phe Thr Leu Phe Phe Leu Leu Phe Phe Cys Phe Val Phe
                    -15
                                       -10
Cys Leu Arg Gly Gln Gly
                1
<210> 868
<211> 110
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<213> Homo sapiens
<220>
<221> SIGNAL
 <222> -19..-1
<400> 868
Met Glu Leu Gly Leu Ser Trp Leu Phe Leu Val Ala Phe Leu Lys Gly
                -15
                                     -10
Val Gln Cys Glu Val Gln Leu Leu Glu Ser Gly Gly Leu Val Gln
Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe
                        20
Ser Ser Tyr Ala Met Leu Trp Val Arg Gln Ala Pro Gly Lys Gly Leu
                    35
Glu Trp Val Ser Gly Ile Ser Ala Gly Ala Asp Asp Thr Tyr Asp Ala
Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Lys
                                70
Ile Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Arg
<210> 869
<211> 60
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -23..-1
<400> 869
Met Ala Val Ser Val Leu Arg Leu Thr Val Val Leu Gly Leu Leu Val
           -20
                                -15
Leu Phe Leu Thr Cys Tyr Ala Asp Asp Lys Pro Asp Lys Pro Asp Asp
Lys Pro Asp Asp Ser Gly Lys Asp Pro Lys Pro Asp Phe Pro Lys Phe
                    15
Leu Ser Leu Leu Gly Thr Glu Ile Ile Glu Asn Ala
<210> 870
<211> 106
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -24..-1
<400> 870
Met Glu Arg Arg Leu Leu Gly Gly Met Ala Leu Leu Leu Gln
                -20
                                    -15
Ala Leu Pro Ser Pro Leu Ser Ala Arg Ala Glu Pro Pro Gln Asp Lys
            -5
Glu Ala Cys Val Gly Thr Asn Asn Gln Ser Tyr Ile Cys Asp Thr Gly
                        15
His Cys Cys Gly Gln Ser Gln Cys Cys Asn Tyr Tyr Tyr Glu Leu Trp
                    30
                                       35
Trp Phe Trp Leu Val Trp Thr Ile Ile Ile Ile Leu Ser Cys Cys
                45
                                    50 ,
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Val Cys His His Arg Arg Ala Lys His Arg Leu Gln Ala Gln Gln Arg

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Gln His Glu Ile Asn Leu Ile Ala Tyr Arg
<210> 871
<211> 37
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -27..-1
<400> 871
Met Val Val Ala Asp Arg Asn Arg Ala Ser Ser Ser Tyr Leu Cys
                           -20
                                                -15
Leu Leu Phe Ser Leu Ser Leu Phe Leu Cys His Glu Thr Val Cys
 -10
                                            1
Asp Arg Ala Thr Cys
                10
<210> 872
<211> 142
<212> PRT
<213> Homo sapiens
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<221> SIGNAL
<222> -19..-1
<400> 872
Met Asp Trp Thr Trp Arg Phe Leu Phe Val Val Ala Ala Ala Thr Gly
             / -15
                                   -10
Val Gln Ser Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys
Pro Gly Ser Ser Val Lys Val Ser Cys Lys Ala Ser Gly Gly Thr Phe
Ser Xaa Tyr Ala Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu
                    35
                                        40
Glu Trp Met Gly Gly Ile Ile Pro Ile Phe Gly Thr Ala Xaa Tyr Ala
                                    55
Gln Lys Phe Gln Gly Arg Val Thr Ile Thr Ala Asp Xaa Ser Thr Xaa
                                70
Thr Xaa Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Xaa
                           85
Tyr Tyr Cys Ala Arg Gly Gln Ala Pro Gly Arg Val Val Pro Leu-
                       100
                                           105
Phe Leu Trp Gly Gln Gly Thr Trp Ser Pro Ser Pro Gln Pro
                    115
<210> 873
<211> 87
<212> PRT
<213> Homo sapiens
<220> '
<221> SIGNAL
<222> -45..-1
<400> 873
Met Thr Tyr Ser Tyr Ser Phe Phe Arg Pro Glu Leu Ile Val Asn His
                   -40
                                       -35
Leu Asn Tyr Val His Ser Glu Ala Asn Arg Arg Thr Lys Thr Lys Thr
```

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Leu Leu Ser Leu Leu Ser Phe Leu Asp Glu Thr Ser Gly Leu Ser Thr
                                - 5
           -10
His Leu Pro Cys Leu Ser Leu Ser Lys Glu Cys Gly Val Leu His Leu
                                           15
                        10
Asp Ile His Gly Lys Lys Glu Asp Met Arg Asp Glu Val Leu Leu Ala
                                        30
                   25
Leu Asn Xaa Cys Thr His Arg
                40
<210> 874
<211> 79
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<213> Homo sapiens
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<222> -19..-1
<400> 874
Met Lys Ser Phe Ser Arg Ile Leu Phe Leu Val Phe Leu Leu Ala Gly
                                   -10
Leu Arg Ser Lys Ala Ala Pro Ser Ala Pro Leu Pro Leu Gly Cys Gly
                                                10
                           5
            1
Phe Pro Asp Met Ala His Pro Ser Glu Thr Ser Pro Leu Lys Gly Ala
                                            25
                        20
   15
Ser Glu Asn Ser Lys Arg Asp Arg Leu Asn Pro Glu Phe Pro Gly Thr
                                       40
                   35
30
Pro Tyr Pro Glu Pro Ser Lys Leu Pro His Thr Val Ser Leu Glu
                                    55
 <210> 875
 <211> 51
 <212> PRT
 <213> Homo sapiens
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 <222> -41..-1
 <400> 875
 Met Arg Val Pro Ile Phe Pro His Pro His Gln Leu Ser Leu Leu Phe
                                             -30 .
    -40
                        -35
 Ile His Leu Phe Ile Tyr Leu Phe Arg Glu Arg Val Ser Leu Cys His
                                        -15
                     -20
 Leu Gly Trp Ser Ala Val Val Gln Ser Gln Pro Thr Thr Leu Thr
                                     1
 Ser Arg Ala
         10
 <210> 876
 <211> 44
 <212> PRT
 <213> Homo sapiens
 <220>
 <221> SIGNAL
 <222> -37..-1
 <400> 876
 Met Trp Lys Glu Ser Ser His Gly Cys Asn Asn Leu Gly Ser Ser Tyr
                                                 -25
     -35
                             -30
 Leu Asp Asp Thr Gly Val Gly Ser Phe Leu Phe Val Leu Phe Cys Phe
```

-15

-20

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Gly Gly Ser Arg Ala Leu Leu Leu Pro Gly Ser Gly
<210> 877
<211> 26
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -16..-1
<400> 877
Met His Thr Phe Leu Cys Leu Leu Phe Tyr Leu Ile Val Ser Cys Gly
                       -10
Ala Val Phe Leu Thr Val Pro Ser Pro Gln
              5
<210> 878
<211> 52
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -39..-1
<400> 878
Met Ala Trp His Pro Thr Pro Pro Pro Leu Xaa Xaa Pro Pro Pro Leu
                                   -30
               -35
Xaa Arg Xaa Ser Leu Pro Ala Cys Ala Asp Ser Ile Ile Leu Xaa Leu
                                -15
          -20
Xaa Phe Pro Gly Ile Leu Gly Gln Ala His Leu Xaa Ser Glu Gln Trp
                            1
       -5
Thr Gln Tyr Leu
<210> 879
<211> 37
<212> PRT
<213> Homo sapiens
<220>
 <221> SIGNAL
<222> -21..-1
 <400> 879
 Met Pro Ile Leu Pro Gln Asp Ile Leu His Leu Leu Ile Leu Leu Ser
                                    -10
                        -15
 -20
 Gly Thr Cys Phe Thr Trp Ile Leu Leu Trp Leu Pro Leu Ser Pro Leu
                              5
 -5
 Leu Gly Leu Lys Cys
            15 .
 <210> 880
 <211> 85
 <212> PRT
 <213> Homo sapiens
 <220>
 <221> SIGNAL
 <222> -20..-1
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<400> 880 Met Lys Ala Leu Gly Ala Val Leu Leu Ala Leu Leu Leu Cys Gly Arg -15 -10 Pro Gly Arg Gly Gln Thr Gln Gln Glu Glu Glu Glu Asp Glu Asp His Gly Pro Asp Asp Tyr Asp Glu Glu Asp Glu Asp Glu Val Glu Glu 20 15 Glu Glu Thr Asn Arg Leu Pro Gly Gly Arg Ser Arg Val Leu Leu Arg 35 Cys Tyr Thr Xaa Xaa Ser Leu Pro Arg Asp Glu Arg Cys Asn Leu Thr Gln Asn Cys Ser His <210> 881 <211> 88 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -15..-1 <400> 881 Met Lys Glu Tyr Val Leu Leu Leu Phe Leu Ala Leu Cys Ser Ala Lys -5 -10 Pro Phe Phe Ser Pro Ser His Ile Ala Leu Lys Asn Met Met Leu Lys 10 25 Asp Asp Glu Asp Asn Ser Leu Phe Pro Thr Arg Glu Pro Arg Ser His 40 Phe Phe Pro Phe Asp Leu Phe Pro Met Cys Pro Phe Gly Cys Gln Cys 55 Tyr Ser Arg Val Val His Cys Ser 70 <210> 882 <211> 95 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -19..-1 <400> 882 Met Lys His Leu Trp Phe Phe Leu Leu Leu Val Ala Ala Pro Arg Trp -15 -10 Ala Met Ser Gln Val Gln Leu Gln Glu Ser Gly Pro Arg Leu Val Lys Pro Ser Gly Thr Leu Ser Leu Thr Cys Ser Val Ser Gly Gly Ser Met 20 Ala Thr Ser Asp Trp Trp Ser Trp Phe Arg Gln Thr Pro Glu Lys Gly 35 Leu Glu Trp Ile Gly Glu Ile Phe Gln Thr Gly Pro Thr Asn Tyr Asn 55 50 Pro Ser Leu Lys Ser Arg Val Ser Met Ser Val Asp Met Ser Lys . 70 <210> 883

<211> 129

<212> PRT

WO 99/53051 458 <213> Homo sapiens <220> <221> SIGNAL <222> -26..-1 <400> 883 Met Asp Leu Thr Cys Lys Lys Met Lys His Leu Trp Phe Phe Leu Leu -20 -15 Leu Val Ala Ala Pro Arg Trp Ala Leu Ser Gln Leu Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu Thr Leu Ser Leu Thr Cys 15 Thr Val Ser Gly Glu Ser Ile Thr Thr Asn Ser Phe Cys Trp Ala Trp 30 Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Leu Gly Thr Val Cys 45 Tyr Gly Gly Thr Thr Tyr Xaa Asn Xaa Ser Leu Lys Ser Arg Val Lys 60 65 Leu Ser Leu Asp Thr Ser Thr Asn Gln Phe Ser Leu Lys Val Thr Ser 75 80 Met Thr Ala Gly Asp Ala Ala Val His Tyr Cys Ala Gly Leu Arg Val 95 Ser <210> 884 <211> 66 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -63..-1 <400> 884 Met Ala Asn Gly Thr Asn Ala Ser Ala Pro Tyr Tyr Ser Tyr Glu Tyr -60 -55 Tyr Leu Asp Tyr Leu Asp Leu Ile Pro Val Asp Glu Lys Lys Leu Lys -35 -45 -40 Ala His Lys His Ser Ile Val Ile Ala Phe Trp Val Ser Leu Ala Ala -25 -20 Phe Val Val Leu Leu Phe Leu Ile Leu Leu Tyr Met Ser Trp Ser Ala -15 -10 Ser Pro <210> 885 <211> 133 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -19..-1 <400> 885 Met Asp Trp Thr Trp Arg Phe Leu Phe Val Val Ala Ala Ala Thr Gly -15 -10

Val Gln Ser Gln Xaa Xaa Leu Xaa Gln Ser Gly Ala Glu Val Lys Lys

Pro Gly Ser Ser Val Lys Val Ser Cys Xaa Ala Ser Gly Gly Ile Xaa

Ser Xaa Tyr Ser Phe Asn Trp Val Arg Gln Ala Pro Gly Gln Gly Phe

25

40

20

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459
Glu Trp Leu Gly Arg Ile Ile Pro Ile Leu Gly Ile Thr Asn Tyr Ala
                                    55
Glu Lys Phe Arg Gly Arg Leu Thr Ile Thr Val Asp Lys Ser Thr Arg
                                70
Val Val Tyr Met Glu Gln Ser Ser Leu Thr Ser Ala Asp Thr Ala Val
                           85
Tyr Tyr Cys Ala Lys Pro Thr Met Thr Ser Glu Leu Arg Val Tyr Tyr
                        100
    95
Gln Xaa Thr Leu Trp
<210> 886
<211> 30
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -22..-1
<400> 886
Met Trp Asn Arg Tyr Phe Val Phe Tyr Leu Leu Leu Ser Ala Phe
                            -15
 . -20
Thr Ser Gln Thr Val Ser Gly Gln Arg Lys Lys Gly Pro Arg
<210> 887
<211> 142
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -19..-1
<400> 887
Met Lys His Leu Gly Phe Phe Leu Leu Leu Val Ala Ala Pro Arg Trp
                                     -10
                -15
Val Leu Ser Gln Leu Gln Leu Gln Glu Ser Gly Ser Gly Leu Glu Lys
 Pro Ser Gln Thr Leu Ser Leu Thr Cys Ser Val Ser Gly Gly Ser Ile
 Ser Ser Asp Asp Leu Ser Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys
                                         40
 Gly Leu Glu Trp Ile Gly Tyr Ile Tyr Gln Asn Glu Arg Thr Leu Tyr
                                     55
                 50
 Asn Pro Ser Leu Lys Ser Arg Ala Ala Ile Ser Val Asp Arg Ser Lys
                                 70
 Asn Gln Phe Ser Leu Lys Leu Thr Ser Val Thr Ala Ala Asp Met Ala
                             85
 Val Tyr Tyr Cys Ala Thr Ser Val Met Xaa Ser Phe Gly Gly Val Leu
                         100
 Val Pro Asn Leu Phe Leu Thr Thr Gly Ala Arg Glu Ser Arg
                     115
 <210> 888
 <211> 155
 <212> PRT
 <213> Homo sapiens
 <220>
 <221> SIGNAL
 <222> -19..-1
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<400> 888
Met Lys His Leu Trp Phe Phe Leu Leu Leu Val Ala Gly Pro Arg Trp
                                    -10
                -15
Val Leu Ser Gln Val Gln Leu Xaa Glu Ser Gly Pro Arg Leu Val Lys
Pro Ser Gln Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Ala Ser Val
Ser Ser Arg Gly Tyr Tyr Trp Thr Trp Ile Arg Gln Leu Pro Gly Lys
                    35
Gly Leu Glu Trp Ile Gly Tyr Ile Xaa Tyr Thr Gly Ser Thr Phe Tyr
                                     55
                50
Asn Pro Ser Leu Lys Ser Arg Leu Thr Ile Ser Ile Asp Thr Ser Lys
                                70
            65
Asn Gln Phe Ser Leu Asn Leu Arg Ser Val Thr Thr Ala Asp Thr Ala
                             85
Val Tyr Tyr Cys Ala Arg Asp His Phe Asp Leu Leu Phe Asp Pro Trp
                        100
Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro
                                         120
                   115
Ser Val Phe Pro Leu Ala Xaa Ser Ser Lys Ser
                130
<210> 889
<211> 63
<212> PRT
 <213> Homo sapiens
<220>
 <221> SIGNAL
 <222> -41..-1
 <400> 889
 Met Ala Cys Arg Glu Arg Pro Arg Pro Leu Leu Trp Arg Ser Arg Gly
                        -35
 Arg Phe Phe Asn Trp Gly Lys Leu Phe Phe Cys Phe Val Leu Xaa Leu
                     -20
 Phe Cys Phe Val Phe Glu Ala Glu Ser Arg Ser Val Ala Gln Ala Gly
                -5
 Val Gin Trp Arg Tyr Phe Gly Ser Leu Gln Ala Leu Pro Pro Trp
 <210> 890
 <211> 25
 <212> PRT
 <213> Homo sapiens
 <220>
 <221> SIGNAL
 <222> -21..-1
 <400> 890
 Met His Glu Phe Ile Ser Gly Phe Phe Ile Leu Phe His Trp Ser Leu
                         -15
 Cys Leu Cys Leu Cys Gln Tyr His Ala
 <210> 891
 <211> 44
  <212> PRT
  <213> Homo sapiens
  <220>
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<221> SIGNAL
<222> -42..-1
<400> 891
Met Ala Tyr Ala Ile Ser Pro Phe His Ser Ser Trp Asn Pro Leu Phe
                           -35
Thr Ser His Lys Ala Ser Ala Ser His Ser His Leu Gly Leu Leu Val
                        -20
Cys Leu Phe Ala Val Thr Ser Ile Leu Cys Ser Ser
<210> 892
<211> 60
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -15..-1
<400> 892
Met Ser Pro Val Leu Leu Leu Ala Leu Leu Gly Phe Ile Leu Pro Leu
                    -10
                                       - 5
Pro Gly Ser Ala Xaa Ala Xaa Ser Ala Ser Leu Gly Gln Phe Ser Met
                                10
Cys Gly Arg Cys Pro Thr Cys Pro Gly Asn Gly Pro Leu Arg Thr Pro
Ala Ala Thr Xaa Xaa Xaa Val Pro Gly His Val Asp
<210> 893
<211> 154
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -23..-1
<400> 893
Met Ala Thr Ala Met Asp Trp Leu Pro Trp Ser Leu Leu Phe Ser
                                -15
            -20
Leu Met Cys Glu Thr Ser Ala Phe Tyr Val Pro Gly Val Ala Pro Ile
       -5
Asn Phe His Gln Asn Asp Pro Val Glu Ile Lys Ala Val Lys Leu Thr
                    15
Ser Ser Arg Thr Gln Leu Pro Tyr Glu Tyr Tyr Ser Leu Pro Phe Cys
                                    35
                30
Gln Pro Ser Lys Ile Thr Tyr Lys Ala Glu Asn Leu Gly Glu Val Leu
                                50
Arg Gly Asp Arg Ile Val Asn Thr Pro Phe Gln Val Leu Met Asn Ser
                            65
Glu Lys Lys Cys Glu Val Leu Cys Ser Gln Ser Asn Lys Pro Val Thr
                        80
Leu Thr Val Glu Gln Ser Arg Leu Val Ala Glu Arg Ile Thr Glu Asp
                                       100
Tyr Tyr Val His Leu Ile Ala Asp Asn Leu Pro Val Ala Thr Gly Trp
                                   115
               110
Ser Ser Thr Pro Thr Glu Thr Ala Met Thr
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<210> 894 <211> 28

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<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -18..-1
<400> 894
Met Pro Ser Pro Cys Leu Ile Ser Leu Leu Gln Cys Ala His Val Ser
                                -10
           -15
Leu Gly Leu Gln Tyr Pro Cys Xaa Leu Leu Leu Pro
                        5
<210> 895
<211> 53
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -17..-1
<400> 895
Met Asn Leu Ser Leu Val Leu Ala Ala Phe Cys Leu Gly Ile Ala Ser
                            -10
    -15
Ala Val Pro Lys Phe Asp Gln Asn Leu Asp Thr Lys Trp Tyr Gln Trp
                                        10
Lys Ala Thr His Arg Arg Leu Tyr Gly Ala Asn Glu Glu Gly Trp Arg
            20
Arg Ala Ala Trp Glu
            35
<210> 896
<211> 85
<212> PRT
<213> Homo sapiens
<220>
 <221> SIGNAL
 <222> -19..-1
 <400> 896
 Met-Glu Phe Gly Leu Asn Trp Val Phe Leu Val Ala Ile Phe Thr Gly
                                    -10
                -15
Val His Cys Glu Val Gln Leu Val Glu Ser Gly Gly Asp Leu Val Gln
            1
 Pro Gly Arg Ser Leu Arg Leu Ser Cys Thr Ala Ser Gly Phe Thr Phe
                        20
                                             25
 Gly Asp Tyr Ala Met Thr Trp Phe Arg Gln Ala Ser Gly Lys Arg Leu
                                        40
                    35
 Glu Trp Leu Gly Phe Ile Arg Asn Arg Gly Ser Gly Gly Ser Ala Glu
                 50
 Tyr Gly Ala Ser Val
             65
 <210> 897
 <211> 51
 <212> PRT
 <213> Homo sapiens
 <220>
 <221> SIGNAL
 <222> -17..-1
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<400> 897
Met Lys Asn Cys Leu Leu Ile Leu Leu Met Leu Leu Leu Phe Ala Ile
        -15
                            -10
His Ile Asn Arg Met Asn Val Arg Asn Val Gly Asn Thr Leu Val Val
Val Gln Ile Leu Phe Ser Ile Arg Val Phe Ile Leu Glu Arg Asn Pro
                 20
                                     25
Leu Asn Val
<210> 898
<211> 149
 <212> PRT
 <213> Homo sapiens
<220>
 <221> SIGNAL
 <222> -19..-1
 <400> 898
Met Glu Leu Gly Leu Ser Trp Ile Phe Leu Leu Ala Ile Leu Lys Gly '
                -15
                                    -10
Val Gln Cys Glu Val Gln Leu Val Glu Ser Gly Gly Leu Val Gln
                            5
Pro Gly Arg Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe
                        20
Asp Asp Tyr Ala Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu
                    35
                                         40
. Glu Trp Val Ser Gly Ile Thr Trp Asn Ser Gly Xaa Ile Gly Tyr Ala
                                     55
Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn
Ser Leu Tyr Leu Gln Met Asn Ser Leu Arg Thr Glu Asp Thr Ala Phe
                            85
Tyr Phe Cys Ala Lys Ala Arg Gly Leu Phe Ser Asp Thr Trp Pro Tyr
                        100
                                             105
Xaa His Tyr Ala Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val
Ser Ser Ala Ser Thr
<210> 899
<211> 25
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -14..-1
<400> 899
Met Leu Leu Val Phe Phe Val Leu Trp Thr Cys Ser Leu Ala Leu Leu
                -10
Ala Ser Ser Pro Ile Ala Ala Xaa Pro
        5
<210> 900
 <211> 127
 <212> PRT
 <213> Homo sapiens
 <221> SIGNAL
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<222> -19..-1 <400> 900 Met Asp Trp Thr Trp Arg Ile Leu Leu Leu Val Ala Ala Ala Thr Asp -10 -15 Ala Ser Ser Gln Met Gln Leu Leu Gln Ser Gly Pro Glu Val Lys Lys Thr Gly Ser Ser Val Lys Leu Ser Cys Thr Ala Ser Gly Asp Thr Leu 20 Ala Tyr His Tyr Leu His Trp Val Arg Gln Ala Pro Gly Gln Ala Leu 35 Glu Trp Met Gly Trp Ile Thr Pro Phe Ser Gly Asp Thr Asn Phe Ala 50 55 Gln Arg Phe Gln Asp Arg Leu Thr Phe Thr Arg Asp Arg Ser Met Ser 70 Thr Val Tyr Met Thr Leu Thr Ser Leu Ile Ser Glu Asp Thr Ala Met 85 Tyr Tyr Cys Ala Thr Asp Gly Arg Arg Thr Asn Arg Leu Phe Glu 100 <210> 901 <211> 68 -<212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -18..-1

<400> 901 Met Ala Gly Gln Leu Leu Gly Cys Leu Leu Trp Leu Leu Thr His Ile -15 Lys Ala Gln Asp Ser Val Arg Asp Ala Tyr Trp Lys Thr Gly Ser Cys Pro Pro Pro Phe Leu His Val Ser Thr Phe Xaa Xaa Lys Leu Thr Phe 25 20 , Ser Thr Lys Gly Asn Leu Leu His Ser Ile Pro Leu Ser Ser Pro Leu

Ala Cys Val Leu

<210> 902 <211> 105 <212> PRT <213> Homo sapiens

<220> <221> SIGNAL <222> -91..-1

<400> 902 Met Lys Glu Ala Val Pro Pro Gly Cys Thr Lys Ser Pro Ser His Phe -85 Ser Glu Gly Phe Asp Arg Trp Ala Leu Glu Glu Thr Pro Pro Glu Asn -65 -70 Leu Ile Gly Ala Leu Leu Ala Ile Phe Gly His Leu Val Val Ser Ile -50 -55 Ala Leu Asn Leu Gln Lys Tyr Cys His Ile Arg Leu Ala Gly Ser Lys -35 Asp Pro Arg Ala Tyr Phe Lys Thr Lys Thr Trp Trp Leu Gly Leu Phe -20 Leu Met Leu Leu Gly Glu Leu Gly Val Phe Ala Ser Tyr Ala Phe Ala

465 Pro Leu Ser Leu Ile Val Pro Leu Ser . 10 <210> 903 <211> 44 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -18..-1 <400> 903 Met Ala Phe Leu Trp Leu Leu Ser Cys Trp Ala Leu Leu Gly Thr Thr -10 -15 Phe Gly Cys Gly Val Pro Ala Ile His Pro Gly Cys Gln Leu Ser Pro 5 1 Arg Leu Pro Pro Thr Leu Leu Pro Thr Glu Arg Gly 20 <210> 904 <211> 82 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -20..-1 <400> 904 Met Ala Pro Phe Gln Asn Phe Leu Trp Leu Phe Phe Val Leu Asn Leu -15 -10 Gly Ser Phe Ala Phe Ser Ser Xaa Pro Asn Ser Leu Phe Tyr Thr Ile 1 10 His Phe Gly Pro Asn Phe Phe Thr Leu Leu Tyr Lys Gln Gly Ala Glu 15 20 Met Cys Val Tyr Val Phe Asn Phe Leu Tyr Pro Phe Ala Leu Gly Tyr 35 40 Phe Phe Ser Tyr Asp Ile Leu Asp Leu Pro Val Xaa Val Arg Pro Pro 50 55 45 Ser Gly <210> 905 <211> 54 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -35..-1 Met Asp Phe Thr Gln Cys His Ser Leu Leu Leu Arg Val Glu Tyr Ser -30 -25 Pro Val Ser Val Cys Phe Leu Leu Ser Val Ala Phe Asn Gln Leu -15 -10 Val Phe Ala Leu Tyr Pro Ile Gln Ala Thr Xaa Cys Phe Ser Xaa Val 5 Ser Leu Pro Phe Pro Ala

<210> 906 <211> 23

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466
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -15..-1
<400> 906
Met Leu Leu Leu Leu Ala Cys Gly Val Pro Ser Leu Trp Pro Phe
-15 -10
Ala Leu Ala Leu Leu Lys Thr
<210> 907
<211> 43
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -23..-1
<400> 907
Met Phe Ile Glu Asn Ile Gly Leu Lys Phe Ser Phe Leu Leu Leu His
          -20
                               -15
Leu Cys Gln Val Leu Leu Ser Arg Arg Ala Gly Thr Ile Pro Thr Glu
 -5
                          1
Thr Ile Pro Lys Lys Leu Arg Arg Arg Asp Gly
                   15
<210> 908
<211> 105
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -24..-1
<400> 908
Met Gln Asn Arg Thr Gly Leu Ile Leu Cys Ala Xaa Ala Leu Leu Met
               -20
                                   -15
Gly Phe Leu Met Val Cys Leu Gly Ala Phe Phe Ile Ser Trp Gly Ser
Ile Phe Asp Cys Gln Gly Ser Leu Ile Ala Ala Tyr Leu Leu Pro
                       15
Leu Gly Phe Val Ile Leu Leu Ser Gly Ile Phe Trp Ser Asn Tyr Arg
                   30
Gln Val Thr Glu Ser Lys Gly Val Leu Arg His Met Leu Arg Gln His
                                   50
Leu Ala His Gly Ala Leu Pro Val Ala Thr Val Asp. Ser Ala Ala Leu
           60
                               65
Leu Lys Ile Met Cys Lys Gln Leu Leu
<210> 909
<211> 52
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
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<222> -44..-1

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<400> 909
Met Lys Val Glu Gly Glu Glu Lys Leu Tyr Arg Leu Leu Arg Ser Gly
               -40
                                  -35
Asp Leu Phe Lys Phe His Gln Pro His Phe Tyr Glu Leu Ser Gly Leu
           -25
                               -20
Thr Cys Thr Ser Ser Leu Leu Ser Phe Ala Leu Gly Arg Ser Ile Pro
       -10
                           - 5
Gly Ser Phe Pro
<210> 910
<211> 60
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -19..-1
<400> 910
Met Glu Ser Arg Thr Leu Leu Leu Phe Ser Gly Ala Val Ala Leu
              -15
                                  -10
Ile Gln Thr Trp Ala Gly Glu Cys Gly Val Gly Arg Glu Lys Ala Ser
                           5
Ala Gly Arg Ser Glu Gly Pro Ala Arg Arg Ser Lys Ser Ala His Ile
                      20
Xaa Asn Tyr Arg Leu Gln Leu Gln Ser Arg Gln Gly
                  35
<210> 911
<211> 35
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -16..-1
<400> 911
Met Ser Asn Ser Val Pro Leu Leu Cys Phe Trp Ser Leu Cys Tyr Cys
 -15 -10
                                          -5
Phe Ala Ala Gly Ser Pro Val Pro Phe Gly Pro Glu Gly Arg Leu Glu
                                  10
Asp Lys Leu
<210> 912
<211> 52
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -14..-1
<400> 912
Met Pro Trp Thr Ile Leu Leu Phe Ala Ala Gly Ser Leu Ala Ile Pro
               -10
                                  -5
Ala Pro Ser Ile Arg Val Val Pro Pro Tyr Pro Ser Ser Gln Glu Asp
                           10
Pro Ile His Ile Ala Cys Met Ala Ala Gly Asn Phe Pro Gly Ala Asn
                       25
Phe Thr Leu Tyr
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35
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<210> 913
<211> 67
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -64..-1
<400> 913
Met Ala Glu Gly Glu Arg Val Cys Ala Ser Val Val Pro Ser Ala Leu
                                   -55
Arg Thr Leu Lys Arg Arg Ser Asn Leu Ser Arg Ile Pro Ala Gly Gln
                                -40
Glu Lys Glu Gly Lys Ser Arg His Val Ala Pro Pro Phe Arg Phe Phe
                            -25
                                                -20
Pro Phe Ser Gly Phe Leu Phe Phe Gly Phe Leu Phe Pro Val Phe Ser
                        -10
Phe Pro Ser
<210> 914
<211> 71
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -13..-1
<400> 914
Met Phe Cys Leu Ala Ala Ile Leu Ala Ser Ala Ser Ala Gln Arg Phe
                                -5
Pro Ser Ala Phe Ser Pro Ser Pro Phe Xaa Trp Leu Xaa Gln Cys Xaa
                       10
                                            15
Thr Ala Thr Ser Leu Gly Phe Xaa Thr Val Cys Xaa Asn Ser Ile Ile
                   25
                                       30
Ser Leu Trp Tyr Leu Xaa Gly Val Pro Pro Glu Val Xaa Glu Leu Pro
               40
                                    45
Phe Phe Pro Tyr Cys Ser Met
<210> 915
<211> 93
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -17..-1
<400> 915
Met Val Asp Gly Thr Leu Leu Leu Leu Ser Glu Ala Leu Ala Leu
        -15
                           -10
                                                -5
Thr Gln Thr Trp Ala Gly Ser His Ser Xaa Lys Tyr Phe His Thr Ser
                                        10
Val Ser Arg Xaa Gly Arg Gly Glu Pro Arg Phe Ile Ser Val Gly Tyr
                20
                                    25
Val Asp Asp Thr Arg Ser Glu Tyr Trp Asp Arg Glu Thr Arg Ser Ala
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40 Arg Asp Thr Ala Gln Ile Phe Arg Val Asn Leu Arg Thr Leu Arg Gly

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469
                            55
Tyr Tyr Asn Gln Ser Glu Ala Gly Ser Xaa Thr Leu Gln
<210> 916
<211> 75
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -27..-1
<400> 916
Met Asn Phe Arg Gly Pro Gln Thr Phe Ser Leu Ser His Ser Leu Val
                            -20
Leu Ser Leu Ile Ser Leu Ser Ile Ala Trp Ser Met Val Glu Met Xaa
Thr Ser Ala Ser Tyr Lys Gln Lys Phe Ala Leu Arg Ile Leu Val Val
                                    15
                10
Gln Leu Pro Thr Trp Val Glu Cys Pro Val Asn His Arg Cys Ala Leu
           25
Gly Arg Lys Asn Cys Ser Ile Arg Thr Gln Pro
<210> 917
<211> 25
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -20..-1
<400> 917
Met Thr Gly Ile Ser Ile Cys Ser Cys Ile Cys Leu Phe Leu Pro Ser
                 - 15
                                        -10
Leu Ile His Ser Phe Pro Pro Pro Cys
                1
<210> 918
<211> 98
<212> PRT
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<400> 918
Met Asp Leu Leu Cys Lys Asn Met Lys His Leu Trp Phe Phe Leu Leu
                        -20
                                            -15
Leu Val Ala Ala Pro Arg Trp Val Gln Leu Gln Glu Ser Gly Pro Arg
                   - 5
                                        1
Leu Val Arg Pro Pro Glu Thr Leu Lys Pro Ser Glu Thr Leu Ser Leu
                                15
Thr Cys Thr Ile Ser Gly Asp Ser Met Ser Ser Ala Ser Tyr Tyr Trp
                            30
Ala Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Phe Ile Gly Arg
                        45
                                            50
Ala Leu Tyr Ser Gly Thr Thr Asp Tyr Asn Pro Ser Leu Ser Ser Arg
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Ile Thr

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<210> 919
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 <212> PRT
 <213> Homo sapiens
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 <222> -45..-1
 <400> 919
 Met Ser Ser Glu Lys Ser Gly Leu Pro Asp Ser Val Pro His Thr Ser
                     -40
                                         -35
 Pro Pro Pro Tyr Asn Ala Pro Gln Pro Pro Ala Glu Pro Pro Ala Pro
              -25
                                     -20
 Pro Leu Ser Leu Ser Leu Cys Leu Ser Leu Cys His Thr His Thr His
            -10
                                 -5
 Thr His Thr His
   5
 <210> 920
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 <222> -28..-1
 <400> 920
 Met Thr Pro Ala Leu Arg Cys Ala Phe Ala Leu Ala Ile Ala Gly Leu
                                 -20
 Val Ser Leu Leu Met Gln Pro Glu Gly Ala Leu Gly Glu Glu Ala Ala
   -10
                            - 5
· Ser Ala Ala Ala Gln Gly Arg Gln Leu Ala Glu Leu Arg Leu
                    10
 <210> 921
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 <222> -38..-1
 <400> 921
 Met Ser Gly Leu Phe Pro Val Pro Val Arg Val Asn Val Asp Ile Ala
             -35
                                -30
                                                     -25
 Gln Asn Ile Thr Cys Ser Ser Phe Ser Leu Leu Ile Phe Leu Ser
        -20
                             -15
                                                 -10
 Phe Pro Tyr Thr Leu Cys Ile Leu Tyr Arg Val Lys Ser Tyr Thr Pro
                        1 ·
 Thr Glu Ser Ile Thr Ala Phe Asn Leu Thr Ile Gly Xaa Phe Pro Tyr
 Leu Xaa Xaa Ser Thr Pro
             30
 <210> 922
 <211> 39
 <212> PRT
 <213> Homo sapiens
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<220>
 <221> SIGNAL
 <222> -33..-1
 <400> 922
Met Cys Arg Ala Ala Cys Ile Ile Arg Met Ala Val Arg Ile Ser Phe
            -30
                               -25
 Phe Leu Ser Tyr His Ala Leu Ser Leu Cys Leu Cys Thr Cys Ala Phe
  -15
Ala Phe Leu Ser Leu Leu Gly
    1
                   5
 <210> 923
 <211> 59
 <212> PRT
 <213> Homo sapiens
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 <222> -17..-1
 <400> 923
Met Lys Phe Leu Leu Xaa Ala Leu Gly Phe Leu Xaa Gln Val Asn
     -15
               -10
                                               -5
 Pro Xaa Pro Ile Xaa Gly Gly Ser Lys Met Cys Glu Xaa His Pro Arg
                  5
                                       10
Ile Leu Gln Asp Met Leu Pro Leu Gly Gly Asp Ser Ile Val His Val
               20
                                   25
Gln Arg Xaa Gln Lys Met Leu His Gln Leu Leu
            35
<210> 924
<211> 105
<212> PRT
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<221> SIGNAL
<222> -42..-1
<400> 924
Met Val Pro Trp Val Arg Thr Met Gly Gln Lys Leu Lys Gln Arg Leu
      -40
                           ~35
                                              -30
Arg Leu Asp Val Gly Arg Glu Ile Cys Arg Gln Tyr Pro Leu Phe Cys
                       -20
                                          -15
Phe Leu Leu Cys Leu Ser Ala Ala Ser Leu Leu Leu Asn Arg Tyr
                   -5
                                      1
Ile His Ile Leu Met Ile Phe Trp Ser Phe Val Ala Gly Val Val Thr
          10
                              15
Phe Tyr Cys Ser Leu Gly Pro Asp Ser Leu Leu Pro Asn Ile Phe Phe
                           30
Thr Ile Lys Tyr Lys Pro Lys Gln Leu Gly Leu Gln Glu Leu Phe Pro
                       45
Gln Gly His Ser Cys Ala Val Cys Gly
<210> 925
<211> 43
<212> PRT
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<221> SIGNAL
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472
<222> -34..-1
<400> 925
Met Ala Trp Gly Ser Pro Gly Lys Ile Phe Leu Met Gly Phe Leu Gly
                -30
                                   -25
Gly Glu Leu Val Phe Leu Leu Cys Leu Phe Xaa Leu Phe Phe Phe Ser
       . -15
                              -10
Phe Leu Lys Arg Ser Phe Ala Leu Glu Cys Asn
<210> 926
<211> 28
<212> PRT
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<222> -16...-1
<400> 926
Met Phe Phe Ser Ile Leu Leu Leu Leu Ala Pro Pro Leu Pro Ser Ala
                    -10
                                          - 5
Val Ser Leu Leu Pro Phe Phe Phe Tyr Cys Val Gln
               5
                                   10
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<211> 42
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<222> -22..-1
<400> 927
Met Val Asp Phe Ile Leu Arg Ser Leu Leu Leu Val Cys Ser Trp Leu
                                    -10
 -20
                           -15
Ser Ile Ser Leu His Ala His Thr Thr Ala Phe Cys Thr Tyr Ser Lys
 -5
            . 1
Lys Ile His Thr Val Met Ser Phe Phe Cys
               15
<210> 928
<211> 26
<212> PRT
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<400> 928
Met Arg Ser Leu Leu Tyr Phe Leu Cys Val Ser Ser Tyr Val Thr Ser
                       -10
Phe Phe Phe Phe Phe Phe Phe Phe
                                   10
                5
<210> 929
<211> 68
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473
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Met Pro Phe Ile Ser Phe Leu Cys Leu Ile Ala Leu Ala Gly Thr Ser
                          -5
                   -10
Ser Thr Met Leu Arg Ser Ala Leu Ala Gly Thr Ser Ser Thr Met Xaa'
Xaa Arg Ser Gly Xaa Ser Gly Xaa Pro Xaa Leu Val Xaa Val Leu Arg
                           25
Gly Asn Ala Phe Ser Phe Phe Pro Phe Ser Leu Met Xaa Ala Met Gly
                       40
Cys His Arg Trp
50
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<400> 930
Met Tyr Thr Phe Leu Leu Gly Ala Ile Phe Ile Ala Leu Ser Ser
 -15
                     -10
Arg Ile Leu Leu Val Lys
<210> 931
<211> 44
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<221> SIGNAL
<222> -42..-1
<400> 931
Met Cys Leu Cys Pro Cys Trp Asp Val Phe Thr Val Phe Val Cys Val
                           -35
Ser Val Cys Val Ser Val Ser Val Pro Val Gly Met Tyr Leu Val Cys
                       -20
Val Cys Val Cys Val Cys Xaa Cys Xaa Arg
                   -5
<210> 932
<211> 50
<212> PRT
<213> Homo sapiens
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<221> SIGNAL
<222> -34..-1
<400> 932
Met Leu Ile Ala Lys Gln Ala Gln Pro Gln Gly Leu Thr Ala Ile Cys
                                   -25
              . -30
Phe Pro Leu Thr Pro Leu Phe Ser Leu Leu Met Leu Thr Gln Ser Pro
           -15
                               -10
                                                   -5
Leu Ala Gly Gln Glu Gly Arg Glu Gly Gly Lys Glu Arg Tyr Leu Leu
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Val Ile
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 <210> 933
 <211> 62
 <212> PRT
 <213> Homo sapiens
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 <221> SIGNAL
 <222> -26..-1
 <400> 933
 Met Leu Arg Thr Trp Ser Ser Leu Pro Trp Thr Arg Phe Arg Val Cys
                         -20
                                              -15
 Leu Leu Ser Leu Ser Leu Phe Leu Trp Ala Asn Arg Leu Glu Asp Ser
                     -5
 Arg Ser Cys Gln Pro Asn Pro Met Ser Leu Thr Thr Leu Pro Gly His
             10
                                15
 Arg Leu Lys Glu Ala Val Trp Leu Pro Ala Pro Ser Leu Gly
                             30
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 <211> 72
 <212> PRT
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 <222> -29..-1
 <400> 934
 Met Ala Pro Phe Leu Arg Gln Val Asp Xaa Trp Gly Ala Gln Ala Gly
                 -25
                                    -20
 Leu Val Val Xaa Trp Leu Leu Pro Xaa Gln Cys Ser Cys Glu Arg Ser
                                 ~5
 Glu Gln Tyr Leu Ser Thr Cys Leu Pro Gln His Ser Ser Ile Lys Gln
                         10
 Ser Cys Ile Lys His Pro Ala Gly Pro Ile Pro Ala Gly His Leu Gln
                     25
 Gly Lys Ala Thr Ala Ala Pro Leu
<210> 935
 <211> 73
~<212> PRT
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 <222> -19..-1
 <400> 935
 Met Glu Phe Gly Leu Lys Trp Leu Phe Leu Val Ala Ile Leu Lys Gly
                 -15
                                     -10
 Val Arg Cys Glu Val Lys Leu Val Glu Ser Gly Gly Leu Val Gln
 Pro Gly Gly Ser Leu Arg Leu Ser Cys Val Gly Ser Gly Phe Val Phe
 Asp Lys Tyr Gly Ile Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu
                    35
Gln Trp Val Ala Gly Ile Gly Gly Gly
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<210> 936
<211> 128
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -16..-1
<400> 936
Met Ala Leu Ala Met Leu Val Leu Val Val Ser Pro Trp Ser Ala Ala
                        -10
Arg Gly Val Leu Arg Asn Tyr Trp Glu Arg Leu Leu Arg Lys Leu Pro
                                    10
Gln Ser Arg Pro Gly Phe Pro Ser Pro Pro Trp Gly Pro Ala Leu Ala
                                25
Val Gln Gly Pro Ala Met Phe Thr Glu Pro Ala Asn Asp Thr Ser Gly
                            40
Ser Lys Glu Asn Ser Ser Leu Leu Asp Ser Ile Phe Trp Met Ala Ala
                        55
Pro Lys Asn Arg Arg Thr Ile Glu Val Asn Arg Cys Arg Arg Asn
                    70
Pro Gln Lys Leu Ile Lys Val Lys Asn Asn Ile Asp Val Cys Pro Glu
                                    90
Cys Gly His Leu Lys Gln Lys Xaa Val Leu Cys Ala Thr Ala Met Lys
                                105
<210> 937
<211> 30
<212> PRT
<213> Homo sapiens
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<221> SIGNAL
<222> -20..-1
<400> 937
Met Phe Phe Tyr Ser His Phe Leu Leu Phe Pro Leu Ser Leu Leu
                   -15
                                        -10
Phe Thr Leu Gly Phe Leu Phe Val Phe Phe Phe Phe Phe Phe
<210> 938
.<211> 101
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<213> Homo sapiens
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<222> -46..-1
<400> 938
Met Lys Gln Ser Lys Arg Xaa Met Val Lys Arg Arg Arg Ser Pro Ala
Leu Gly Glu Glu Arg Phe Ser Pro Ser Ser Ile Leu His Pro Arg Leu
                    -25
                                        -20
Pro Leu Val Leu Leu Gly Thr Arg Val Pro Leu Ser Gly Gly Gly Pro
                -10
                                    -5
Gly Glu Pro Asp Gln Gly Arg Ser Ala Pro Ser Trp Lys Ser Leu Ala
                            10
Ser Thr His Xaa His Ser Arg Pro Ala Ala Gly Ala Thr Pro Ala Arg
```

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Pro Ala Thr Gln Ser Gln Leu Gly Pro Phe Ala Pro Pro Leu Pro Gly
                                         45
Val Arg Pro Ala Pro
<210> 939
<211> 32
<212> PRT
<213> Homo sapiens
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<221> SIGNAL
<222> -18..-1
<400> 939
Met Leu Leu Glu Ser Leu Cys Val Leu Ser Leu Leu Val Ser Phe Lys
                                -10
Ser Ala Cys Leu Thr Arg Glu Pro Ala Phe Asp Ser Gln Ala Arg Pro
       1
<210> 940
<211> 94
<212> PRT
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<222> -46..-1
Met Val Phe Gly Tyr Trp Lys Gln Pro Leu Ile Thr Leu Ala Lys Lys
Ser Val Lys Cys Ala Arg Glu Cys Leu Arg Cys Ser Leu Arg Pro Leu
                    -25
                                         -20
Val Leu Leu Tyr Leu Ser Phe Ala Ala Leu Gly Val Val Ala Leu Arg
                -10
                                    -5
Ser Val Glu Ser Pro Leu Ala Glu Thr His Ser Cys Trp Leu Ser Leu
                            10
Gly Met Cys Val Leu Gln Cys Glu Gln Gln Trp Val Pro Thr Pro Val
                        25
Ser Phe Leu Cys Gly Leu Ser Gly Ser Ser Thr Ile Ile Val
<210> 941 .
<211> 66
<212> PRT
<213> Homo sapiens
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<221> SIGNAL
<222> -24..-1
<400> 941
Met Cys Val Val Cys Ser Val His Gly Val Cys Cys Val Tyr Val Val
                -20
                                    -15
Cys Leu Val Ser Cys Val Leu Cys Val Val Cys Pro Val Cys Trp Val
Met Cys Cys Val Trp Cys Ile Cys Val Cys Val Trp Cys Val Cys Cys
Met Cys Cys Val Leu Ser Cys Val Val Ser His Gly Leu Cys Gly Val
Ser Trp
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<210> 942
<211> 59
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
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<400> 942
Met Glu Leu Gly Leu Ser Trp Val Phe Leu Val Ala Val Leu Glu Val
               -15
                       -10
Val Gln Cys Glu Ile Gln Leu Ile Asp Ala Gly Gly His Val Gln
Ala Gly Gly Ser Leu Arg Leu Ser Cys Val Ala Ser Asp Phe Leu Phe
                      20
Arg Ser Tyr Trp Met Thr Trp Val Arg His Pro
                  35
<210> 943
<211> 41
<212> PRT
<213> Homo sapiens
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<221> SIGNAL
<222> -39..-1
<400> 943
Met Ser Ile Leu Leu Arg Val Leu Gly Ile Lys Gly Cys Trp Ile Leu
            -35
                                  -30
Ser Asn Pro Phe Ser Ala Cys Ile Glu Met Ile Leu Leu Phe Leu Phe
 -20
                               -15
Leu Ile Leu Phe Ile Trp His Ile Arg
-5
<210> 944
<211> 27
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -25..-1
<400> 944
Met Ala Glu Lys Ala Gly Ser Thr Phe Ser His Leu Leu Val Pro Ile
                 -20
                                -15
Leu Leu Leu Ile Gly Trp Ile Val Gly Cys Thr
               -5
<210> 945
<211> 34
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -19..-1
<400> 945
Met Ala Glu Ser Arg Gly Arg Leu Tyr Leu Trp Met Cys Leu Ala Ala
               -15
```

-10

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478
 Ala Leu Ala Ser Phe Leu Met Gly Phe Met Val Gly Trp Phe Ile Lys
                            5
 Pro Leu
    15
 <210> 946
 <211> 40
 <212> PRT
 <213> Homo sapiens
 <220>
 <221> SIGNAL
 <222> -26..-1
 <400> 946
 Met Leu Thr Ser Leu Pro Phe Leu Leu Pro Thr Ile Ser Phe Leu Leu
                        -20
 Leu Leu Tyr Phe Phe Xaa Ile Ala Val Thr His Pro Ser Val Leu Ile
                 -5
 Asn Phe Ser Phe Ser Phe Pro Arg
            10
 <210> 947
 <211> 36
 <212> PRT
 <213> Homo sapiens
<220>
<221> SIGNAL
 <222> -20..-1
<400> 947
Met Arg Lys Asp Val Arg Phe Leu Leu Phe Phe Thr Cys Gly Leu Pro
        -15 -10
Ala Leu His Gly Asp Ser Arg Val Glu Cys Ser Lys Ala His Pro Pro
                              5
Ala Met Tyr Tyr
       15
<210> 948
<211> 48
<212> PRT
<213> Homo sapiens
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<221> SIGNAL
<222> -27..-1
<400> 948
Met Leu Phe Trp Leu Pro Ser Pro Ser Glu Thr Thr Ser Ala Trp Thr
                           -20
Leu Leu Ser Ile Ser Leu Ser Val Phe Trp Ser Glu Pro Phe Asn Lys
                       -5
                                           1
Ser Leu Gly Ser Ser Lys Leu Pro Cys His Phe Phe Ser Ile Lys Arg
               10
<210> 949
<211> 65
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
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WO 99/53051
                                      479
<222> -47..-1
<400> 949
Met Pro Val Cys Phe Tyr Ser Leu Ile Cys Phe Phe Ile Tyr Phe Cys
                            -40
Leu Leu Ser Pro Arg Glu Thr Ile Glu Glu Val Ala Leu Phe Gln Phe
                    - 25
                                            -20
Ser Leu Leu Xaa Leu Gly Glu Gly Leu Thr Phe Leu Cys Leu Cys Gln
                    -10
                                        -5
Val Met Thr Asn Xaa Met Gln Leu Leu Phe Leu Ser Gly Val Val Cys
                                10
Gly
<210> 950
<211> 21
<212> PRT
<213> Homo sapiens
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<221> SIGNAL
<222> -13..-1
<400> 950
Met Ala Pro Leu Leu Ser Leu Ser Cys Ser Phe Ser Cys His Val
           -10
                               -5
Thr Leu Leu Pro Arg
  5
<210> 951
<211> 47
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -20..-1
<400> 951
Met Val Pro Ala Ala Gly Ala Leu Leu Trp Val Leu Leu Leu Asn Leu
                   -15
                                   -10
Gly Pro Arg Ala Ala Gly Ala Gln Gly Leu Thr Gln Thr Pro Thr Glu
Met Gln Arg Val Ser Leu Arg Phe Gly Gly Pro Met Thr Arg Arg
<210> 952
<211> 58
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -24..-1
<400> 952
Met Val Phe Trp Glu Ile Ser Val Gln Ile Ile Leu Ile Ser Glu Leu
               -20
                                   -15
```

Met Val Phe Trp Glu Ile Ser Val Gln Ile Ile Leu Ile Ser Glu Leu

-20

-15

-10

Leu Leu Leu Arg Ser Val Thr Ser His Asn Thr Met Met Arg Ala Leu

-5

Ser Ser Gln Met Leu Ser Gln Ser Phe Pro Arg Pro Ser Phe Gly Phe

10

15

20

Ile Ser Lys Ile His Pro Ser His Pro Pro
25

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<210> 953
 <211> 74
 <212> PRT
 <213> Homo sapiens
 <220>
 <221> SIGNAL
 <222> -51..-1
 <400> 953
 Met Phe Phe Leu Asn Ile Ala Met Phe Ile Val Val Met Val Gln Ile
                         -45
                                            -40
 Cys Gly Arg Asn Gly Lys Arg Ser Asn Arg Thr Leu Arg Glu Glu Val
 -35
                    -30
                                        ~25
 Leu Arg Asn Leu Arg Ser Val Val Ser Leu Thr Phe Leu Leu Gly Met
                -15
                                  -10
 Thr Trp Gly Phe Ala Phe Phe Ala Trp Gly Pro Leu Asn Ile Pro Phe
            1
                          5
 Met Tyr Leu Phe Ser Ile Phe Asn Ser Leu
   15
                        20
 <210> 954
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 <212> PRT
 <213> Homo sapiens
 <220>
<221> SIGNAL
 <222> -17..-1
 <400> 954
 Met Asn Lys His Phe Leu Phe Leu Phe Leu Leu Xaa Xaa Leu Ile Val
       -15
                     -10
 Ala Val Thr Ser Leu Gln Cys Ile Thr Cys His Leu Arg Thr Arg Thr
   3
                                        10
 Asp Arg Cys Arg Arg Gly Phe Gly Xaa Cys Thr Ala Gln Lys Gly Glu
                20
                                    25
 Ala Cys Met Leu Leu Arg Ile His Gln Arg
            35
 <210> 955
 <211> 47
 <212> PRT
 <213> Homo sapiens
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 <221> SIGNAL
 <222> -35..-1
 <400> 955
 Met Tyr Ile Lys Met Glu Ser Val Thr Leu Ser Pro Ala Pro Val Phe
                    -30
                                        -25
 Pro Val Pro Ala Gln Leu Leu Leu Thr Ser His Phe Leu Gly Glu
                -15
                                    -10
 Ser Leu Gly Gly Gly Thr Leu Leu Val Pro Leu Leu Pro Pro Gly
                            5
 <210> 956
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 <212> PRT
 <213> Homo sapiens
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<220>
<221> SIGNAL
<222> -27..-1
<400> 956
Met Xaa Xaa Ala Leu Leu Arg Ser Arg Met Ile Gln Gly Arg Ile Leu
                          -20
Leu Leu Thr Ile Cys Ala Ala Gly Ile Xaa Gly Thr Arg Gln Phe Gly
                      -5
Tyr Asn Leu Ser Ile Ile Asn Asp
               10
<210> 957
<211> 54
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -47..-1
<400> 957
Met Met Gly Xaa Leu Cys Pro Arg Ser Leu Pro Ile Pro Pro Met Ile
    -45
                     -40
Leu Ser Trp Trp Lys Met Gln Trp Lys Pro Leu Ala Leu Glu Asn Phe
                                     . -20
                       -25
Ser Gly Ser Cys Leu Phe Ser Xaa Ala Trp Leu Xaa Cys Xaa Cys His
                   -10
Gly Asp Asp Asp Leu Ser
<210> 958
<211> 48
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -15..-1
<400> 958
Met Gly Leu Leu Gln Leu Leu Ala Phe Ser Phe Leu Gly Asn Ser Val
                   -10
                                       -5
Glu Thr Val Arg Gly Gly Gly Arg Thr Trp Ala Trp Gly Arg Lys Thr
                               10
Gln Lys Leu Ala His Leu Arg Gly Ile Leu Gly Ala Trp Xaa Arg
       20
                           25
<210> 959
<211> 25
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -14..-1
<400> 959
Met Leu Val Leu Val His Ser Ser Leu Ser Lys Thr Leu Ser Gln Lys
              -10
Lys Lys Lys Phe Thr Xaa Pro Thr Arg
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<210> 960
 <211> 48
 <212> PRT
 <213> Homo sapiens
 <220>
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<222> -19..-1
 <400> 960
 Met Ser Phe Ser Ser Ala Leu Ile Leu Val Ile Ser Cys Leu Leu Leu
                 -15
                                     -10
 Ala Phe Glu Cys Val Cys Ser Cys Phe Ser Gly Ser Phe Asn Cys Asp
             1
                            5
                                             . 10
 Val Arg Val Ser Ile Ser Asp Leu Ser Cys Phe Leu Leu Trp Gly Lys
     15
                         20
 <210> 961
 <211> 28
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 <222> -22..-1
 <400> 961
 Met Gly Phe Trp Cys Gly Cys Pro Phe Cys Leu Xaa Val Phe Leu Leu
                             -15
 Thr Asp Arg Thr Leu Ser Cys Arg Ser Val Gly Val
 . -5
 <210> 962
 <211> 27
 <212> PRT
 <213> Homo sapiens
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 <221> SIGNAL
 <222> -15..-1
 <400> 962
Met Val Leu Leu Ser Leu Ser Leu Trp Gly Ile Ser Thr Leu Ser Ser
                     -10
                                         - 5
 Thr Thr Ile Glu Leu Ile Tyr Thr Pro Ile Gly
<210> 963
 <211> 28
<212> PRT
 <213> Homo sapiens
<220>
<221> SIGNAL
<222> -25..-1
Met Ala Ser Leu Leu Ser Gly Phe Thr Ser Phe Cys Leu Leu His Val
                    -20
His Ser Phe Leu Pro Pro Val Phe Ser Thr Gln Asn
                - 5
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<211> 42
<212> PRT
<213> Homo sapiens
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<222> -30..-1
<400> 964
Met Glu Thr Ala Leu Xaa Xaa Thr Pro Gln Lys Arg Gln Val Met Phe
-30
                    -25
Leu Ala Ile Leu Leu Xaa Xaa Trp Glu Ala Gly Ser Glu Ala Val Arg
                -10
Tyr Ser Ile Pro Glu Glu Thr Glu Ser Gly
                            10
<210> 965
<211> 66
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -35..-1
<400> 965
Met Met Leu Asp Phe Ala Leu Ser Pro Arg Leu Glu Arg Ser Gly Leu
                    -30
                                       -25
Ile Met Ala Cys Cys Thr Leu Asp Leu Leu Gly Ser Ser Pro Pro
                                    -10
Thr Ser Ala Ser Gln Val Ala Gly Thr Gly His Val Pro Pro His Pro
Ala Ser Phe Phe Tyr Phe Xaa Val Xaa Gln Val Tyr Tyr Val Ser Gln
 15
                        20
Leu Ile
30
<210>. 966
<211> 64
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -22..-1
<400> 966
Met Arg Thr Pro Gln Leu Ala Leu Leu Gln Val Phe Phe Leu Val Phe
                            -15
                                                -10
Pro Asp Gly Val Arg Pro Gln Pro Ser Ser Ser Pro Ser Gly Ala Val
Pro Thr Ser Leu Glu Leu Gln Arg Gly Thr Asp Gly Gly Thr Leu Gln
               15
                                    20
Ser Pro Ser Glu Ala Thr Ala Thr Arg Pro Ala Val Pro Gly Leu Arg
           30
<210> 967
<211> 46
<212> PRT
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<220>
<221> SIGNAL
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WO 99/53051
                                       484
<222> -21..-1
<400> 967
Met Pro Arg Pro Arg Ala Cys Ala Ser Trp Pro Leu Leu Ala Ala Val
                         -15
Ser Gly Leu Arg Gly Leu Glu Trp Pro Pro Ser Trp Arg Arg Val Val
                    1.
                                    5
Ala Ala Val Gly Val Cys Arg Val Arg Asp Trp Gly Pro Arg
<210> 968.
<211> 23
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -17..-1
<400> 968
Met Asn Gly Ile Phe Leu Leu Leu Ile Ser Val Leu Thr Val Ile Trp
       -15
                            -10
Phe Trp Lys Thr His Pro Gly
   1
<210> 969
<211> 27
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -18..-1
<400> 969
Met Val Phe Leu Val Xaa Leu Leu Cys Ile Ile Xaa Leu Tyr Leu Ile
           -15
                                -10
Arg Gly Ser Glu Trp Xaa Leu Pro Pro Asn Trp
        1
<210> 970
<211> 53
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -18..-1
<400> 970
Met Met Thr Leu Ala Leu Phe Phe Leu Leu Arg Ile Ala Leu Ala Ser
           -15
                               -10
Trp Ala Leu Phe Trp Ile His Met Asn Phe Arg Arg Ala Phe Phe His
                                            10
Leu Arg Trp Phe Asp Ile Asn Ser Thr Glu Ser Val Asn Cys Phe Gly
Gln Tyr Gly Leu Ala
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<210> 971 <211> 37 <212> PRT <213> Homo sapiens

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<220>
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<222> -29..-1
<400> 971
Met Ser Ile Arg Ser Asn Trp Ser Ser Val Glu Ser Lys Ser Arg Ile
               -25
                     -20 -15
Ser Leu Leu Val Phe Cys Leu Asn Asp Leu Ser Asn Ala Val Xaa Xaa
   · -10
Gly Ile Glu Xaa Pro
 5
<210> 972
<211> 120
<212> PRT
<213> Homo sapiens
<221> SIGNAL
<222> -16..-1
<400> 972
Met Ala Trp Ile Pro Leu Phe Leu Gly Val Leu Ala Tyr Cys Thr Gly
                      -10
Ser Val Ala Ser Tyr Glu Leu Thr His Pro Pro Ser Val Ser Val Ser
                                  10
Pro Gly Gln Thr Ala Ser Ile Thr Cys Ser Gly Asp Lys Leu Gly Asp
Lys Tyr Ala Cys Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro Val Leu
                          40
Val Ile Tyr Gln Asp Ser Lys Arg Pro Ser Gly Ile Pro Glu Arg Phe
                      55
Ser Gly Ser Asn Ser Gly Asn Thr Ala Thr Leu Thr Ile Ser Gly Thr
                   70
Gln Ala Met Asp Glu Ala Asp Tyr Tyr Cys Gln Ala Trp Asp Ser Ser
              85
Thr Val Val Phe Gly Gly Gly Thr
           100
<210> 973
<211> 32
<212> PRT
<213> Homo sapiens
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<221> SIGNAL
<222> -29..-1
<400> 973
Met Val Cys Val Ile Phe Lys Glu Leu Met Glu Phe Glu Phe Pro Gly
             -25
                          -20
Phe Cys Phe Xaa Leu Cys Phe Gly Arg Ser Ser Leu Cys Cys Arg Xaa
          -10
                              -5
<210> 974
<211> 78
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -30..-1
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<400> 974
Met Glu Ser Ser Gly Thr Pro Ser Val Thr Leu Ile Val Gly Ser Gly
                    -25
                                         -20
                                                             -15
Leu Ser Cys Leu Ala Leu Xaa Thr Leu Ala Val Val Tyr Ala Ala Leu
                -10
Trp Arg Tyr Ile Arg Ser Glu Arg Ser Ile Ile Leu Ile Asn Phe Cys
                            10
Leu Ser Ile Ile Ser Ser Asn Ile Leu Ile Leu Val Gly Gln Thr Gln
Thr His Asn Lys Glu Tyr Leu His Asn His His Cys Ile Phe
<210> 975
<211> 58
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -31..-1
<400> 975
Met Gly Val Cys Cys Ala Gln Asn Cys Ser Val Ser Gly Xaa Xaa Arg
   -30
                        -25
                                             -20
Asn Ala Leu Xaa Phe Leu Ala Ser Ser Phe Cys Phe Gly Glu Ala Asp
-15
                   -10
                                        -5
Ser Gly Ser Arg Cys Cys Leu Lys Ile Ile Leu Gly Phe Tyr Leu Ile
                                10
Arg Tyr Ser Leu Ile Thr Tyr Gln Val Arg
        20
<210> 976
<211> 40
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -18..-1
<400> 976
Met Lys Ile Leu Tyr Leu Phe Phe Phe Leu Lys Trp Ser His Pro Gly
            -15
                               -10
Trp Ser Ala Thr Xaa Trp Ser Trp His Thr Ala Thr Ser Ala Ser Leu
       3
                        5
Ile Gln Val Ile Leu Pro Pro Trp
                    20
<210> 977
<211> 34
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -26..-1
<400> 977
Met Thr Pro Cys Phe Leu Gln Met Asp Asn Leu Thr Pro Leu Phe Leu
                        -20
                                            -15
Ser Gly Cys Phe Leu Phe Leu Ser Xaa Cys Xaa Ile Tyr Leu Ala Arg
```

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Ile Leu
<210> 978
<211> 48
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -40..-1
<400> 978
Met Gly Ser Ala Gly Arg Leu His Tyr Leu Xaa Met Thr Ala Glu Asn
                   -35
                                       -30
Pro Thr Pro Gly Asp Leu Ala Pro Xaa Pro Leu Ile Thr Cys Lys Leu
                -20
                                    -15
Cys Leu Cys Glu Gln Ser Xaa Gly Gln Asp Asp His Thr Pro Gly Met
                                1
<210> 979
<211> 88
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -49..-1
<400> 979
Met Asn His Leu Pro Pro Asn His Tyr Arg Xaa His Val Phe Thr Cys
               -45
                                   -40
His Val Asp Gln Tyr Leu Thr Val Glu Thr Ala Gly Gly Met Glu Lys
            -30
                               -25
                                                   -20
Glu Ala Val Ser Val Thr Val Leu Leu Ser Ala Ala Pro Cys Leu Leu
       -15
                           -10
                                                -5.
Ser Cys Phe Leu Gly Ser Ser Val Ser Gly Leu Ala Phe Trp Val Ser
 1
                                       10
Gln Gln Lys Thr Lys Gly Pro Glu Arg Cys Lys Asn Thr His His Xaa
         . 20
Ala Xaa Asn Asn Phe Pro Ala Arg
<210> 980
<211>, 42
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -40..-1
<400> 980
Met Asn Lys Ile Lys Glu Asn Thr His Thr His Thr His Thr
                   -35
                                       -30
His Lys Asn Asn Thr Lys Leu Val Ser Asn Leu Phe Leu Phe Met Leu
               -20
                                   -15
Pro Leu Trp Cys Ser Ile Gly Thr Cys Thr
           - 5
<210> 981
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<211> 51 <212> PRT <213> Homo sapiens

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<220>
<221> SIGNAL
<222> -42..-1
<400> 981
Met His Asp Ser Ser Gly Lys Asn Asn Phe Arg Lys Ile Pro Val Val '
               -35
   -40
Asn Leu Ile Tyr Leu Tyr Val Asp Ile His Ile His Lys Leu Phe Leu
                      -20
                                         -15
Tyr Ser Leu Phe Thr Glu Asn Val Leu Ala His Pro Cys Ile Val Leu
            -5
Arg Arg Leu
<210> 982
<211> 37
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -33..-1
<400> 982
Met Gly Arg Leu His Arg Pro Arg Ser Ser Thr Ser Tyr Arg Asn Leu
        -30 -25
Pro His Leu Phe Leu Phe Leu Phe Val Gly Pro Phe Ser Cys Leu
  -15
                          -10
Gly Ser Tyr Ser Arg
   1
<210> 983
<211> 44
<212> PRT
<213> Homo sapiens
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<221> SIGNAL
<222> -27..-1
<400> 983
Met Gln Ser Gln Ala Ala Arg Glu His Lys Pro Gly Xaa Ser Arg Leu
                                   -15
                         -20
Leu Leu Leu Leu Leu Xaa Leu Pro Leu Pro Pro Pro Xaa Leu Arg
                   -5
Thr Arg Xaa Phe Ser Xaa Thr Thr Leu Thr Ala Gly
               10
 <210> 984
 <211> 25
 <212> PRT
 <213> Homo sapiens
 <220>
 <221> SIGNAL
 <222> -15..-1
 <400> 984
 Met Arg Leu Trp Ser Leu Ala Cys Leu Ser Pro Pro Ala Val Gln Leu
               -10
 Gly Ser Gln Gln Ala Thr Asp Trp Trp
          5
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<210> 985
<211> 32
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -25..-1
<400> 985
Met Ser Pro Leu Phe Ile Leu Ile Val Leu Ile Trp Ile Phe Ser Phe
-25 -20
                                -15
Phe Phe Phe Ile Thr Leu Val Arg Gly Ser Ile Asn Leu Phe Phe
             -5`
<210> 986
<211> 25
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -22..-1
<400> 986
Met Asn Leu Gly Gly His Ser Asp His Ser Thr Phe Leu Phe Phe Leu
      -20
                           -15
Phe Phe Ser Val Phe Cys Phe Phe
 -5
<210> 987
<211> 91
<212> PRT
<213> Homo sapiens
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<221> SIGNAL
<222> -21..-1
<400> 987
Met Leu Asp Phe Ala Ile Phe Ala Val Thr Phe Leu Leu Ala Leu Val
                       -15
                                          -10
Gly Ala Val Leu Tyr Leu Tyr Pro Ala Ser Arg Gln Ala Ala Gly Ile
                   1
Pro Gly Ile Thr Pro Thr Glu Glu Lys Asp Gly Asn Leu Pro Asp Ile
           15
                               20
Val Asn Ser Gly Ser Leu His Glu Xaa Leu Val Asn Leu His Glu Arg
       30
                           35
Tyr Gly Pro Val Val Ser Phe Trp Phe Gly Arg Arg Leu Val Val Ser
                       50
Leu Gly Thr Val Asp Val Leu Lys Gln His Arg
                   65
<210> 988
<211> 28
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -18..-1
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<400> 988

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Met Ala His Cys Ser Leu Glu Leu Leu Gly Ser Ser Ser Pro Pro Ile
         -15
                                -10
 Ser Ala Ser Gln Ser Thr Gly Ile Thr Ser Val Ser
 <210> 989
 <211> 44.
 <212> PRT
 <213> Homo sapiens
 <220>
 <221> SIGNAL
 <222> -17..-1
 <400> 989
 Met Pro Ser Gln Leu Leu Leu Ser Leu Ser Leu Phe Leu Phe Phe
      -15
                            -10
 Trp Arg Gln Ser Leu Val Leu Trp Pro Arg Leu Glu Cys Ser Cys Val
                   5
 Ile Ala Ala His Cys Ser Leu Thr Ser Gln Ala Arg
                20
 <210> 990
 <211> 83
 <212> PRT
 <213> Homo sapiens
 <220>
 <221> SIGNAL
 <222> -46..-1
 <400> 990
 Met Tyr Thr Asn Lys Tyr Thr Leu Ile Tyr Asn Ile Leu Ile Tyr Asn
                        -40
                                             -35
 Ile Cys Xaa Xaa Tyr Met Trp Leu Ile Leu Ile Tyr Met Tyr Leu His
                    -25
                                         -20
Ile Cys Leu Phe Cys Cys Xaa Phe Ile Ser Ser Cys Asn Ser Val Phe
                -10
                                     -5
 Pro Cys Val Ile Xaa Phe Leu Leu Pro Glu Glu Leu Leu Xaa Val Xaa
                            10
 Leu Xaa Xaa Yaa Phe Xaa Val Arg Trp Ser Leu Xaa Xaa Ser Ser Arg
                         25
 Leu Glu Cys
 35
 <210> 991
 <211> 35
 <212> PRT
 <213> Homo sapiens
<220>
 <221> SIGNAL
 <222> -31..-1
 Met Leu Leu Thr His Asn Glu Asp Tyr Met Pro Gly Asn Xaa Xaa
                         -25
                                             -20
 Xaa Xaa Leu Trp Ser Leu Ile Gln Ala Val His Ile Cys Leu Gly Arg
                     -10
                                         -5
 Lys Lys Lys
 <210> 992
 <211> 89
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<220>

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<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -19..-1
<400> 992
Met Glu Phe Gly Leu Ser Trp Val Phe Leu Val Ala Ile Ile Lys Gly
               -15
                                   -10
Val Gln Cys Gln Val Gln Leu Val Glu Ser Gly Gly Leu Val Lys
                                               10
Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe
                       20
Ser Asp Tyr Xaa Xaa Thr Xaa Ile Arg Xaa Ala Xaa Gly Lys Gly Leu
                · 35
                                       40
Xaa Trp Ile Xaa Xaa Ile Thr Thr Ser Gly Asn Thr Ala Xaa Tyr Ala
                            . 55
               50
Xaa Ser Val Lys Xaa Arg Phe Thr Ile
           65.
<210> 993
<211> 55
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -17..-1 .
<400> 993
Met Lys Arg Phe Phe Leu Phe Val Cys Leu Xaa Phe Asp Glu Ser Cys
       -15
                          -10
Ser Val Thr Arg Leu Gly Cys Cys Gly Ala Ile Ser Ala His Cys Xaa
                                      10
Leu Arg Leu Pro Gly Ser Ser Xaa Xaa Pro Ala Ser Thr Ser Arg Val
               20
                                  25
Xaa Gly Ile Thr Gly Met Arg
<210> 994
<211> 40
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -38..-1
<400> 994
Met Ser Cys His Ser Leu Leu Ala Cys Lys Val Phe Thr Glu Lys Ser
                               -30
Pro Thr Lys His Ile Arg Glu His His Cys Met Leu Phe Val Ser Phe
                           -15
Leu Leu Leu Leu Gly Ser Arg
   -5
<210> 995
<211> 50
<212> PRT
<213> Homo sapiens
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<221> SIGNAL
 <222> -26..-1
 <400> 995
 Met Thr Ser Ser Val His Leu Leu Val Phe Lys Asp His Leu Leu Ser
                         -20
                                             -15
 Met Leu Ser Cys Cys Gln Gly Ala Cys Cys Pro Ser Thr Pro His Glu
                     - 5
                                         1
 Gly Thr Arg Ser Thr Val Ser Trp Ile Pro Pro Thr Tyr Lys Ala Ala
                                 15
 Thr Gln
 <210> 996
 <211> 23
 <212> PRT
 <213> Homo sapiens
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 <221> SIGNAL
 <222> -19..-1
 <400> 996
 Met Val Arg Ala Ser Ile Leu Leu Ser Met Phe Cys Val Ser His Thr
                 -15
                                      -10
 Val Gln Thr Ala Thr Tyr Thr
             1
 <210> 997
<211> 52
 <212> PRT
 <213> Homo sapiens
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 <222> -17..-1
 <400> 997
 Met Glu Lys Thr Ala Leu Ser Ser Phe Thr Trp Trp Ala Pro Ala Cys
                             -10
        -15
                                                 - 5
 Cys Ala Pro Arg Thr Tyr Val Val Ser Ala Thr Thr Leu Ser Ala Val
 Gln Gly His Cys Pro Leu Gln Ser Arg Thr Ser Thr Lys Gly Lys Leu
                                     25
 Trp Pro Phe Gly
             35
 <210> 998
 <211> 50
 <212> PRT
 <213> Homo sapiens
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 <221> SIGNAL
 <222> -23..-1
 <400> 998
 Met Ile Phe Thr Phe Gln Gln Ile Gly Gly Lys Leu Leu Leu Ser Gly
             -20
                                 -15
 Leu Thr Gln Glu Cys Leu Gly Ala Leu Pro Glu Ala Asn Val Phe Cys
 ·, -5
                             1
 Arg Gly Gly Cys Thr Ala Thr Val Leu Lys His Gly Lys Ala Ser Pro
 10
                     15
 Glu Ser
```

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<210> 999
<211> 46
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -31..-1
<400> 999
Met Asn Cys Val Arg Gln Ala Asn Ile Arg Met Gln Cys Lys Ile Tyr
                        -25
                                           -20
Asp Ser Leu Leu Ala Leu Ser Pro Asp Leu Gln Ala Ala Arg Gly Leu
                    -10
                                        - 5
Met Cys Ala Ala Ser Val Met Ser Phe Leu Ala Phe Met Met
                                 10
<210> 1000
<211> 44
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -40..-1
<400> 1000
Met Ile Trp Leu Ser Phe Cys Leu Leu Leu Val Tyr Arg Asn Ala Cys
                    -35
                                        -30
Asp Phe Cys Thr Leu Thr Leu Tyr Pro Gly Thr Leu Leu Lys Leu Leu
                -20
                                    -15
Ile Ser Leu Arg Ser Phe Trp Ala Glu Thr Thr Gly
<210> 1001
<211> 43
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -25..-1
<400> 1001
Met Phe Ser Ser Pro Gly Leu Arg Thr Leu Phe Val Leu Val Gly Ser
                    -20
                                        -15
Leu His Leu Phe Leu Ser Val Leu Ala Ser Lys Ser Arg Asn Ser Lys
                - 5
Lys Gln Arg Leu Phe Leu Leu Val Pro Leu Tyr
        10
<210> 1002
<211> 51
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -23..-1
<400> 1002
Met Leu Thr Asp Gly Ile Leu Met Arg Val Asn Val Cys Ser Leu Pro
```

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-15
 Ala Pro Gly Leu Cys Ser Gly Gln Pro Gly Val Arg Ala Trp Pro Gly
                           1
 Val Thr Gln Leu Thr Gln Xaa Glu Glu Cys Pro Trp Phe Ser Ala Leu
                    15
                                        20
 Glu Gly Leu
 <210> 1003
 <211> 49
 <212> PRT
 <213> Homo sapiens
<220>
<221> SIGNAL
<222> -33..-1
<400> 1003
Met Phe Asn Trp Asn Pro Trp Leu Thr Thr Leu Ile Thr Gly Xaa Ala
            -30
                                -25
Gly Pro Leu Leu Leu Leu Ser Leu Ile Phe Gly Pro Cys Ile
     -15
                            -10
Leu Asn Ser Phe Leu Asn Xaa Ile Lys Gln Arg Ile Ala Ser Gly Lys
                                   . 10
                                                            15
Arg
<210> 1004
<211> 102
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -29..-1
Met Ala Gly Ser Arg Gln Arg Gly Leu Arg Ala Arg Val Arg Pro Leu
                -25
                                   -20
Phe Cys Ala Leu Leu Ser Leu Xaa Xaa Xaa Pro Xaa Xaa Arg
           -10
                               -5
Arg Xaa Arg Arg Pro Arg Gly Arg Val Ala Thr Ser Pro Phe Arg Val
                       10
Xaa Ile Gln Leu Gln Gly Ala Ala Pro Gly Ala Glu Arg Arg Asp Arg
                   25 ·
Ala Leu Leu Gly Pro Arg Gly Glu Cys Tyr Ser Lys Phe Arg Ser Asn
               40
                                   4'5
Ser Ser Ser Thr Ile Phe Lys Lys Xaa Lys Arg Leu Ser Val Xaa Xaa
           55
Asp Xaa Ser Gly Pro Gly
       70
<210> 1005
<211> 96
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -19..-1
<400> 1005
Met Glu Phe Gly Leu Ser Trp Val Phe Leu Val Ala Ile Leu Lys Gly
               -15
Val His Cys Asp Val Gln Leu Val Glu Ser Gly Gly Leu Val Gln
```

```
Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Leu Thr Leu
                        20
Ser Asn Asp Trp Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu
                                        40
Val Trp Val Ser His Ile Asp Ser Ser Xaa Thr Ile Thr Asn Tyr Ala
                                    55
Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Trp
<210> 1006
<211> 38
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -15..-1
<400> 1006
Met Gly Leu Phe Leu Gly Phe Leu Ala Cys Ser Val Ala Tyr Gln Cys
               -10
His Ser Ala Phe Val Thr Val Ala Ser Gln Tyr Thr Leu Lys Ser Glu
                               10
Thr Leu Met Pro Ala Ala
    20
<210> 1007
<211> 104
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -49..-1
<400> 1007
Met Trp Glu Asp Ser Arg Asn Lys Arg Gly Gly Arg Trp Leu Val Ser
                -45
                                    -40
Leu Ala Lys Gln Gln Arg His Ile Glu Leu Asp Arg Leu Trp Leu Glu
            -30
                                -25
Thr Phe Ser Val Phe Leu Gly Leu Ile Phe Phe Leu Glu Leu Ala Thr
       -15
                            -10
Gly Ile Leu Ala Phe Val Phe Lys Asp Trp Ile Arg Asp Gln Leu Asn
                                        10
Leu Phe Ile Asn Asn Asn Val Lys Ala Tyr Arg Asp Asp Ile Asp Leu
                                    25
Gln Xaa Leu Ile Asp Phe Ala Gln Glu Tyr Trp Ser Cys Cys Gly Xaa
           35
Glu Ala Pro Ile Xaa Gly Thr Gly
        50
<210> 1008
<211> 34
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -14..-1
<400> 1008
Met Phe Leu Ser Leu Ser Thr Ala Phe Trp Val Val Tyr Ala Met Ile
```

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-10
                                     - 5
Ile Tyr Ser Ala Leu Ser Ala Gly Phe Ile Ile Phe Phe Leu Val Val
                            10
Phe Asn
    20
<210> 1009
<211> 38
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -34..-1
<400> 1009
Met Tyr Ile Val Met Asp Leu Pro Leu Trp Leu Ser His Glu Val Gln
                                    -25
Ser Tyr Ile Pro Ser Phe Phe Leu Phe Phe Cys Phe Glu Thr Gly Ser
                                -10
            -15
His Ser Val Thr His Gly
        1
<210> 1010
<211> 54
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -27..-1
<400> 1010
Met Val Ala His Asp Tyr Gln Asn Ile Ile Ser Leu Phe Phe Leu Ala
                            -20
                                                -15
Phe Ser Phe Ser Phe Pro Ser Ser Phe Ser Ser Phe Phe Leu Xaa
                        -5
                                            1
Phe Leu Ser Phe Phe Ser Ser Phe Phe Leu Ser Leu Leu Ser Phe Pro
                10
Ser Phe Leu Pro Pro Gly
<210> 1011
<211> 136
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -15..-1
<400> 1011
Met Ala Ala Leu Arg Ala Leu Cys Gly Phe Arg Gly Val Ala Ala Gln
                   -10
Val Leu Arg Xaa Gly Ala Gly Val Arg Leu Pro Ile Gln Pro Ser Arg
Gly Val Arg Gln Trp Gln Pro Asp Val Glu Trp Ala Gln Gln Phe Gly
Gly Ala Val Met Tyr Pro Ser Lys Glu Thr Ala His Trp Lys Pro Pro
                        40
Pro Trp Asn Asp Val Asp Pro Pro Lys Asp Thr Ile Val Lys Asn Ile
                                        60
Thr Leu Asn Phe Gly Pro Gln His Pro Ala Ala His Gly Val Leu Arg
```

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70
                                    75
Leu Val Met Glu Leu Ser Gly Glu Met Val Arg Lys Cys Asp Pro His
                               90
Ile Gly Leu Leu His Arg Gly Thr Glu Lys Leu Ile Glu Tyr Lys Xaa
                         105
Tyr Leu Gln Ala Leu Pro Tyr Phe
115
<210> 1012
<211> 50
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -28..-1
<400> 1012
Met Leu Ile Trp Ser Ser Ser Ser Phe Pro Ala Pro Pro Leu Phe Leu
          -25
                               -20
Val Phe Leu His Leu Phe Leu Xaa Val Tyr Leu Gly Leu Val Met Pro
  -10
                           - 5
Thr Gln Gln Tyr Leu Leu Gln Ser Pro Leu Met Phe Thr Asp Lys
                                       15
Ala Gln
<210> 1013
<211> 57
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -46..-1
<400> 1013
Met Cys Arg Met Cys Arg Phe Val Thr Trp Ile Asn Val Cys His Gly
                       -40
                                           -35
Asp Leu Leu His Arg Ser Ser Arg Arg Leu Gly Val Lys Pro Ser Thr
                   -25
                                       -20
His Trp Leu Phe Phe Leu Met Leu Ser Leu Cys Thr Pro Pro Asp Arg
               -10
Pro Trp Cys Val Leu Phe Pro Pro Leu
                    . 10
<210> 1014
<211> 40
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -31..-1
<400> 1014
Met Xaa Thr Gln Glu Ala Gly Leu Ile Phe Phe Ser Pro Pro Phe Ser
                       -25
                                          -20
Leu Ser Leu Ser Leu Pro Leu Ser Leu Xaa Leu Leu Xaa Xaa
                   -10
                                       -5
Pro His Ser Arg Thr Pro Gln Arg
           5
```

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<211> 43
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -13..-1
<400> 1015
Met Glu Phe Leu Leu Trp Ser Leu Xaa Ser Asn Gly Lys Arg Gly
            -10 ·
                               -5
Gln Ala Trp Arg Leu Met Pro Val Val Pro Ala Val Trp Glu Pro Glu
                       10 .
Ala Gly Gly Leu Leu Gln Leu Gly Gly Ser Arg
                    25
<210> 1016
<211> 88
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -37..-1
<400> 1016
Met Met Val Thr Tyr Arg Trp Gly Phe Gly Val Asp Val Xaa Phe Val
     -35
                            -30
Ala Val Asp Ala Ile Pro Phe Cys Leu Leu Val Phe Phe Leu Ile Val
                        -15
                                            -10
Arg Thr Leu Ser Cys Arg Ser Val Gly Val Cys Trp Arg Ser Thr Pro
Asp Pro Val Cys Leu Gly Ile Thr Ser Arg Gly Cys Arg Thr Glu Ile
           15
                               20
Leu Gln Asn Ser Lys Cys Cys Ser Leu Ile Leu Pro Leu Glu Ala Ser
Ser Gln Arg Gly Thr Glu Cys Met
. 45
<210> 1017
<211> 34
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Met Leu Tyr Pro Leu Pro Glu Ile Phe Leu Pro Phe Ser Leu Ser Pro
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Ala Asn Ala Gln Ser Lys Phe Ser Leu Tyr Phe Phe Pro Leu Val Lys
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Pro Gly
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<210> 1018
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<222> -27..-1
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<400> 1018

Met Ser Leu Glu Pro Ala Ser Xaa Leu Leu Gly Val Arg Arg Leu
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Leu Cys Leu Xaa Phe Xaa Arg Leu Leu Gly Thr Ser Leu Leu Lys

Phe Val Xaa Ser Xaa Ser Pro Pro Xaa Pro Xaa Thr Leu Thr Ser Ser 10 15 20

<210> 1019

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<222> -24..-1

<400> 1019

Met Leu Ile Leu Tyr Leu Ala Thr Leu Leu Asn Leu Ser Val Leu Ile'
-20 -15 -10

Leu Cys Val Cys Val Cys Val Tyr Asp Leu Tyr Ile Xaa Arg
-5 1 5

Gly '

<210> 1020

<211> 117

<212> PRT

<213> Homo sapiens

<220>

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<222> -16..-1

<400> 1020

Met Ala Pro Leu Gly Thr Thr Val Leu Leu Trp Ser Leu Leu Arg Ser
-15 -5

Ser Pro Gly Val Glu Arg Val Cys Phe Arg Ala Arg Ile Gln Pro Trp 1 5 10 15

His Gly Gly Leu Leu Gln Pro Leu Pro Cys Ser Phe Glu Met Gly Leu
20 25 30

Pro Arg Arg Phe Ser Ser Glu Ala Ala Glu Ser Gly Ser Pro Glu
35 40 45

Thr Lys Lys Pro Thr Phe Met Asp Glu Glu Val Gln Ser Ile Leu Thr 50 55 60

Lys Met Thr Gly Leu Asn Leu Gln Lys Thr Phe Lys Pro Ala Ile Gln 65 70 75 80

Glu Leu Lys Pro Pro Thr Tyr Lys Leu Met Xaa Gln Ala Gln Leu Glu 85 90 95

Glu Ala Thr Arg Gln 100

<210> 1021

<211> 99

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<222> -34..-1

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500 Met Leu Leu Thr Phe Ser Ser Ser Arg His Arg Arg Leu Tyr Arg -30 -25 -20 Arg Arg Arg His His Leu Leu Phe Val Val Leu Leu Pro Pro Pro -10 -5 -15 Gly Ser Val Xaa Leu Cys Ser Xaa Xaa Xaa Xaa Val Leu Xaa Xaa Xaa Lys Phe Arg Xaa Gly Leu His Gly Ala Met Leu Pro Gly Leu Phe 15 20 Arg Gly Arg Pro Arg Ala Ala Leu Arg Leu Arg Val Ser Pro Xaa Cys 40 Pro Gly Trp Lys Val Ala Arg Ser Arg Leu Thr Ala Thr Ser Ala Ser Arg Xaa Arg 65 <210> 1022 <211> 32 <212> PRT <213> Homo sapiens <220> . <221> SIGNAL <222> -13..-1 <400> 1022 Met Leu Leu Leu Gln Leu Asn Leu Lys Thr Leu Ser Ser Ser Thr -10 - 5 Ile Ala Leu Lys Lys Ile Ser Gly Glu Leu Leu Arg Lys Arg Lys Arg . 10 ·<210> 1023 <211> 18 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -15..-1 <400> 1023 Met Ser Leu Phe Val Leu Leu Ile Ile Thr Gln Leu Leu Tyr Gly Gly -15 -10 Ile Leu <210> 1024 <211> 34 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -28..-1 <400> 1024 Met Asn Cys Phe Cys Asn Phe Val Lys Thr Ser Glu Ala Tyr Met Ile -25 -20 -15 Leu Phe Leu Gly Val Leu Leu Ser Ala Ser Asp Leu Cys Val Tyr Pro Ile Gly <210> 1025

<211> 33

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Met Ser Val Ile Leu Ala Leu Trp Glu Ala Glu Ala Gly Gly Ser Pro
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                                   - 5
Glu Ile Gly Ser Ser Gly Pro Ala Ala Pro Thr Trp Arg Ser Pro Val
                            10
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Gln
<210> 1026
<211> 61
<212> PRT
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<222> -29..-1
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Met Tyr Gly Glu Ser Thr Leu Phe Ile His Ser Ser Val His Gly His
                -25
                                   -20
Leu Gly Cys Leu Leu Leu Ala Val Arg Ser Ser Ala Thr Val Asn Ile
           -10
                             -5
Thr Tyr Xaa Xaa Val Cys Val Asp Ile Xaa Xaa His Phe His Met Leu
                       10
                                           15
Met Ser Gly Ile Thr Gly Ser Tyr Gly Asn Ser Leu Ser
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Met Ala Ala Ser Val Leu Asn Thr Val Leu Arg Arg Leu Pro Met Leu
                        -45
                                           -40
Ser Leu Phe Arg Gly Ser His Arg Val Gln Val Thr Leu Arg Lys Thr
                    -30
                                        -25
Phe Cys Thr Thr Ser Ser Trp Leu Tyr Leu Leu Glu Val Val Ala Pro
                -15
                                    -10
Leu Ser Gly Ile His Glu Trp Arg Pro Ser His Val Cys Leu Ser Cys
            1
                          5
Leu Gly Ser Thr Ser Cys Asn Pro Pro Glu
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Met Leu Arg Ser Ala Cys Val Ser Gln His Ala Gly Gly Ile Trp Val
                    -60
                                        -55
Asp Arg Gly Gly Pro Gln Cys Gln Arg Val Phe Thr Phe Cys Arg Gly
                -45
                                   -40
Leu Ser Pro Asn Phe Gly Arg Ser Glu Thr Gln Arg Glu Arg Trp Ile,
    -30
                                -25
                                                    -20
Arg Pro Gly Gln Leu Met Val Val Ala Glu Thr Ser Gln Gly Ser Trp
                 -10
                                                - 5
Ser Ala Pro Thr Ser Pro Xaa Thr Ser Cys Pro Pro Pro Asn Thr Xaa
                                        10
Thr Thr Pro Xaa
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Met Val Ser Arg Ser Leu Arg Gly Arg Arg Thr Trp Val Arg Cys Met
                    -40
                                        -35
Arg Arg Leu Pro Pro Ile Pro Ala Trp Ser Gln Gly Lys Gly Met Pro
               -25
                                    -20
Gly Phe Val Ser Leu Leu Val Val His Ala Ala Asp Ala Trp Val Ala
           -10
                               -5
Gln Arg Leu Ser Thr Pro Tyr Phe Ser Leu Phe Leu Ser Ile Pro Arg
                       10
Cys Ser Phe Pro Arg Arg Ser Ile Asp Arg Thr Cys Ser Ser Xaa Leu
                  25
                                       30
Asp Ser Glu Gly Ser Ser Ser Ile Xaa Pro Ser Thr Pro Phe
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Met Val Gly Ala Leu Pro Pro Ala Ser Leu Leu Pro Cys Ser Leu Ile
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                                           -10
Ser Asp Cys Cys Ala Ser Asn Glu Arg Gly Ser Met Gly Val Gly Pro
Ser Glu Pro Arg Arg Gly
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<222> -20..-1
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Met Ile Ile Leu Ile Asn Gln Leu Leu Phe Ile Cys Pro Pro Pro
                                      -10
                  -15
Pro Ile Ser Ala Ser Ser Asn Tyr His Phe Thr Leu Tyr Leu His Asp
              1
                            5
Ile Asn Phe Phe Ser
  15
<210> 1036
<211> 18
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Met Thr Asp Val Leu Leu Gln Leu Leu Leu Arg Val Cys Ser Pro Arg
                  -10
Thr Arg
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Met Gly Leu Phe Leu Cys Cys Ser Leu Leu Ile Phe Cys Leu Val Val
        -10
                              - 5
Leu Ile Ile Thr Glu Leu Gly Tyr Gly
 5
                       10
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<221> SIGNAL
<222> -14..-1
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Met Gly Ser Trp Ala Leu Thr Trp Leu His Pro Ala Glu Ala Gly Thr
                         -5
               -10
Arg Val Pro Phe Cys Ser Trp Glu Lys Ser Asp Gly Arg Ser
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<210> 1039

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Met Met Leu Xaa Xaa Xaa Arg Gly Tyr Pro His Arg Thr Glu Arg Tyr
                            -35
        -40
Asp Gly Phe Leu Lys Tyr Ser Asp Pro Asn Asp Ile Ala Leu Ser Val
                        -20
                                             -15
Leu Ser Leu Val Ile Asn Phe Ser Trp Ser Arg Lys Cys Phe Val Pro
                                         1
                    -5
Tyr Tyr Ile Pro Phe Lys Pro Tyr Arg Xaa Pro Tyr Pro Thr Ala Ala
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Arg
<210> 1040
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Met Tyr Val Cys Ile Tyr Ile Xaa Leu Xaa Asp Leu Tyr Asp Phe Phe
                                     -30
                -35
Leu Leu Gly Thr Tyr Phe Phe Glu Arg Lys Cys Phe Val Cys Xaa Leu
                                 -15
            -20
 Phe Val Phe Leu Leu Ser Gly Leu Asn Tyr Phe Ser Ile Leu Ser Phe
                             1
        - 5
 Tyr Pro Arg
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 Met Cys Ile Phe Cys Leu Phe His Leu Leu Tyr His Lys Leu Leu Ser
                     -35
                                         -30
 Arg Ser Leu Phe Phe Cys Cys Ile Phe Ser Gly Phe Ile Thr Phe Ile
                 -20
                                     -15
 Phe Ser Phe Ser Phe Cys Glu Cys Ile Val Gly Met Tyr Ile Tyr Gly
             - 5
 Ala Arg
     10
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Met Xaa Ile Cys Tyr Asn Ile Phe Gln Asn Ile Leu Gly Leu Leu
                                         -15
                      -20
Ile Phe Leu Tyr Leu Ser Leu Asn Leu Phe Cys Ile Phe Phe Ser Val
                                          1
                        - 5
Pro Ala Leu Gln Pro Arg Arg Leu
                10
<210> 1043
<211> 29
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<222> -26..-1
<400> 1043
Met Ala Ser Ser Met Leu Xaa Ser Phe Gln Thr Phe Met Met Leu Thr
                                            -15
                        -20
Leu Leu Gly Phe Pro Ser Lys Ala Leu Thr Phe Ile Ser
                    -5
<210> 1044
<211> 33
<212> PRT
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<222> -20..-1
<400> 1044
Met Gly Arg Ser Lys Arg Gln Leu Leu Ser Leu Pro Gly Ser Phe Ile
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                    -15
-20
Pro Gly Asn Cys Arg Pro Arg Ile Leu Ser Asn Gly Glu Xaa Arg Arg
                                                    10
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Lys
 <210> 1045
 <211> 48
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 <222> -25..-1
 <400> 1045
 Met Arg Ser Asp Gly Phe Ile Arg Gly Phe Cys Phe Cys Phe Leu
                                        -15
                     -20
 Ile Phe Leu Leu Pro Pro Leu Pro Ala Met Ile Leu Arg Pro Leu Gln
                                   1
                - 5
 Pro Cys Gly Ile Ile Ser Pro Ile Lys Pro Leu Phe Pro Phe Phe
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 <210> 1046
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<210> 1050

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<222> -16..-1
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Met Asn Thr Leu Trp Thr Ala Ser Ser Leu Pro Leu Ser Thr His Ser
                    -10
                                           -5
Gln Arg Thr Met Ile His Trp Asn Val Phe Leu Trp Asn Ser Phe Tyr
                                    10
Ser Cys Ile Lys Ile Phe Pro
          20
<210> 1047
<211> 46
<212> PRT
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<222> -31..-1
<400> 1047
Met Thr Trp Thr Lys Cys Pro Leu Pro Leu Gly Pro Ala Phe Phe Thr
                        -25
                                            -20
Gln Cys Cys Leu Ile Gly Leu Leu Val Pro Leu Leu Gly Trp Gly Asn
                   -10
                                       - 5
Gln Asn Thr Gln Trp Tyr Pro Thr Ser Lys Met Pro Asp Gly
            5
                                10
<210> 1048
<211> 37
<212> PRT
<213> Homo sapiens
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<222> -32..-1
<400> 1048
Met Gly Arg Ser Asn Asp Phe Arg Phe Ala Phe Leu Thr Cys Phe Leu
       -30
                     -25
                                                -20
Gly Trp Glu Ile Val Tyr Phe Leu Val Leu Leu Arg Val Leu Tyr Thr
                        -10
 -15
Leu Gln Trp Gly Gly
                5
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Met Lys Thr Asp Asn Leu Thr Ser Phe Leu Thr Tyr Met Pro Leu Ile
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Ser Ser Ser Cys Ser Ile Ala Pro
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Met Arg Phe Arg Phe Cys Gly Asp Leu Asp Cys Pro Asp Trp Val Leu
                                    -70
                -75
Ala Glu Ile Ser Thr Leu Ala Lys Met Ser Ser Val Lys Leu Arg Leu
                                -55
           -60
Leu Cys Ser Gln Val Leu Lys Glu Leu Leu Gly Gln Gly Ile Asp Tyr
                                                -35
                            -40
Glu Lys Ile Leu Lys Leu Thr Ala Asp Ala Lys Phe Glu Ser Gly Asp
                                            -20
                        -25
Val Lys Ala Thr Val Ala Val Leu Ser Phe Ile Leu Ser Ser Ala Ala
                                            ٠.
                                        -5
                    -10
Lys His Ser Val Asp Gly Glu Ser Leu Ser Ser Glu Leu Gln Gln Leu
                                10
Gly Leu Pro Lys Glu His Ala Ala Ser Leu Cys Arg Cys Tyr Glu Glu
                            25
Lys Gln Ser Pro Leu Gln Lys His Leu Arg Val Cys Ser Leu Arg Met
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Asn Arg
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 Met Phe Leu Ala Ala Leu Phe Thr Val Ala Lys Ile Trp Lys Gln Pro
                                     -5
             -10
 Lys Cys Ser Ser Thr Asn Lys Trp Thr Lys Lys Met Trp Tyr Ile Tyr
                                                 15
                             10
 Thr Met Glu Tyr Tyr Ser Ala Ile Lys Lys Asp Asp Ile Leu Ser Phe
                         25
 Ala Thr Ile Trp Met Glu Leu Glu Ser Ile Thr Leu Ser Glu Ile Ser
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 Gly Xaa Pro Lys Asp Lys Leu Leu Met Phe Ser Leu Ile Cys Gly
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  <400> 1052
  Met Glu Ser Ser Thr Phe Ala Leu Val Pro Val Phe Ala His Leu Ser
                                                 -15
                      -20
         -25
  Ile Leu Gln Ser Leu Val Pro Ala Ala Gly Ala Xaa Ser Pro
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Met Gly Cys Leu Leu Ala Ser Glu Tyr Pro Leu Ser Glu Pro Trp Ala
          -75
                             -70
Pro Gly Pro Phe Thr Gln Tyr Leu Val Asp His His His Thr Leu Leu
                         -55
                                           -50
 -60
Cys Asn Gly Tyr Trp Leu Ala Trp Leu Ile His Val Gly Glu Ser Leu
                     -40
                                        -35
Tyr Ala Ile Val Leu Cys Lys His Lys Gly Ile Thr Ser Gly Arg Ala
-30 -25
                          -20
Gln Leu Leu Trp Phe Leu Gln Thr Phe Phe Phe Gly Ile Ala Ser Leu
                                -5
           -10
Xaa Ile Leu Ile
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<400> 1054
Met Cys Cys Trp Ile Trp Val Ala Ser Ile Leu Leu Arg Ile Phe Ala
-15 -10
Ser Val Leu Ile Arg Asp Ile Tyr Leu Trp Phe Ser Phe Phe Phe
                                 10
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Met Ile Ser Ser His Leu Tyr Asn Phe Ser Leu Leu Phe Phe Xaa Leu
                         -15
          -20
Trp Leu Arg Tyr Lys Glu Ser Gly Arg Glu Gly Asn Cys Glu Glu Gly
  -5
                      1
Ala Phe Ser Arg Trp
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 Met Gly Trp Gln Arg Leu Leu Leu Pro Arg Pro Pro Ala Ser Thr
        -15
                            -10
 Gly Ala Ser Asn Ala Thr Arg Xaa Pro Lys Xaa Leu Tyr Arg Xaa Tyr
    1
                    5
                                        10
 Asn His Gly Val Leu Lys Ile Thr Ile Cys Lys Ser Cys Gln Lys Pro
                20
                                    25
                                                        30
 Val Asp Lys Tyr Ile Glu Tyr Asp Pro Val Ile Ile Leu Xaa Asn Ala
            35
                                40
 Ile Leu Cys Lys Ala Xaa Ala Tyr Arg His Ile Leu Phe Asn Thr Gln
                           • 55
 Ile Asn Asn Lys Leu Pro Ile Leu Leu Ala Phe Leu Pro Ser Cys Gly
                        70
 Xaa Thr Ala His Asp Gly Lys Lys Lys Pro Asn Phe Ile Leu Leu Leu
                   85
 Lys Xaa Tyr Tyr Leu Ala Thr Glu Asn
                 100
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 <222> -19..-1
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 Met Ala Ala Gly Val Ser Leu Leu Ala Leu Val Val Arg Val Ile Leu
                -15
                                   -10
 Ser Thr Ala Ile Leu Cys Pro Ser Gly Ala Ser Arg Arg Gln Arg Ser
 Ser Glu Val Glu Trp Gly Thr Asp Ser
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<222> -15..-1
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 Met Asn Pro Leu Phe Trp Leu Ile Leu Cys Ser Gly Leu Leu Cys Asn
 -15
                    -10
 Lys Ser Phe
 <210> 1059
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<222> -18..-1

<400> 1059

Met Arg Gly Ala Trp Ile Ser Ile Phe Leu Ser Ser Leu Ser Leu Ser

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Leu Ser Leu Phe
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<222> -24..-1
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Met Ser Gln Lys Arg Leu Asp Phe Ile Tyr Gln Leu Phe Val Leu Leu
             -20
                                  -15
Pro His Phe Phe Leu Ser Phe Leu Ser Pro Phe Tyr Leu His Pro Trp
                              1
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<211> 52
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<400> 1061
Met Tyr Leu Tyr Leu Leu Ser Ile Cys Met Ser Ser Leu Lys Lys Cys
         -30 -25
Leu Phe Lys Phe Leu Ala His Phe Leu Ile Gly Leu Thr Val Cys Phe
 -15
                        -10
                                             -5
Gly Glu Gly Xaa Leu Met Ser Tyr Arg Ser Ser Tyr Leu Leu Leu Lys
                                   10
                  5
   1
Gly Pro Pro Gly
<210> 1062
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Met Gly Phe Trp Cys Glu Cys Pro Phe Cys Leu Leu Val Phe Leu Leu
                          -15
Thr Glu Trp Thr Ser Ser Lys Leu Gln Lys Thr
                      1
<210> 1063
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<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -22..-1
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Met Trp Trp Gly Arg Cys Phe Ile Arg Val Leu His Leu Phe Pro Leu
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-15

-20

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Thr Pro Ala Ser Thr Gly His Trp
<210> 1064
<211> 58
<212> PRT
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<220>
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<222> -29..-1
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Met Arg Asp Pro Leu Ala Asp Met Val His Ser Tyr Leu Ser Ser Ser
                                    -20
                -25.
Leu Phe Met Ala Leu Pro Pro Val Leu Ser Ser His Gly Ser Arg Asn
                                -5
            -10
Leu Arg Ile Trp Gly Ser Pro Phe Gly Gly Ala Leu Thr Lys Gly Lys
                       10
Ala Pro Pro Thr Pro Ala Gln Pro Ala Leu
                    25
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Met Ser Ser Ala Trp Leu Cys Leu Pro Cys Ser Leu Cys Val Ser Gln
    -15
                            -10
Leu Leu Pro Ser Tyr Ser Leu Leu Ile Pro Ala Pro
   1
<210> 1066
<211> 27
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<221> SIGNAL
<222> -21..-1
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Met Ser Pro Met Trp Ala Gly Leu Leu Ser Leu Leu Gly Pro Leu Xaa
                       -15
 -20
 Pro Pro Met Arg Ala Cys Ser Val Cys Val Leu
                    1
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 <211> 39
 <212> PRT
 <213> Homo sapiens
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 <221> SIGNAL
 <222> -18..-1
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 Met Ser Leu Asn Glu Leu Ser Ile Ala Asp Leu Leu Pro Ser Ser Ser
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513
           -15
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Phe Ala Asn Pro Lys Leu Ser Gly Pro Ile Ser Ile Ser Val Thr Ser
                    5
    1
Ala Gly Ser Pro Pro Gly Ala
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<221> SIGNAL
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<400> 1068
Met Lys Asp Leu Leu Gly Thr Ala Phe Leu Glu Gly Ser Leu Ala Ala
            -10
Tyr Leu Thr Met Ala Asn Ile Thr His Val
<210> 1069
<211> 29
<212> PRT
<213> Homo sapiens
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<221> SIGNAL
<222> -19..-1
<400> 1069
Met Ala Asn Asp Ile Lys His Leu Phe Met Cys Leu Leu Thr Ile Cys
               -15
                                  -10
Ile Ser Ser Leu Glu Lys Leu Pro Phe Phe Phe Phe
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<212> PRT
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<222> -24..-1
<400> 1070
Met Tyr Gln Lys Val Thr Ser Tyr Cys Arg Ser Ala Thr Leu Val Gly
               -20
                                  -15
Phe Thr Val Gly Ser Val Leu Gly Gln Ile Leu Val Ser Val Ala Gly
           - 5
                               1
Trp Ser Leu Phe Ser Leu Asn Val Ile Ser Leu Thr Cys Val Ser Val
                       15
                                           20
Ala Phe Ala Val Ala Trp Phe Leu Pro Met Pro Gln Lys Ser Leu Phe
                   30
                                       35
Phe His His Ile Pro Ser Thr Cys Gln Arg Val Asn Gly Ile Lys Val
                                  50
Gln Asn Gly Gly Ile Val Thr Asp Thr Gln Leu Leu Thr Pro Ser Trp
                               65
Leu Gly
<210> 1071
<211> 19
<212> PRT
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<213> Homo sapiens
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<222> -17..-1
<400> 1071
Met Met Pro Pro Ala Leu Phe Phe Leu Leu Arg Ile Ala Trp Leu Leu
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Gly Leu Phe
  1
<210> 1072
<211> 38
<212> PRT
<213> Homo sapiens
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<221> SIGNAL
<222> -21..-1
<400> 1072
Met Asn Cys Val Thr Leu Ile Gln Ala Leu Ser Leu Trp Ala Ser Val
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                                            -10
Ser Pro Ser Trp Met Cys Arg Pro Pro Ala Ser Phe Ile Ile Thr Thr
-5
Thr Thr Thr Cys Gly
           15
<210> 1073 .
<211> 19
<212> PRT
<213> Homo sapiens
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<221> SIGNAL
<222> -16..-1
<400> 1073
Met Leu Ser Leu Leu Ser Leu Met Ala Arg Thr Asp Leu Val Phe Cys
   -15
                       -10
Ser Pro Arg
<210> 1074
<211> 255
<212> PRT
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<222> .-34..-1
<400> 1074
Met Val Gly Glu Ala Gly Arg Asp Leu Arg Arg Arg Ala Val Ala
               -30
                                    -25
Val Thr Ala Glu Lys Met Ala Val Leu Ala Pro Leu Ile Ala Leu Val
           -15
                               -10
Tyr Ser Val Pro Arg Leu Ser Arg Trp Leu Ala Gln Pro Tyr Tyr Leu
                       5
                                            10
Leu Ser Ala Leu Leu Ser Ala Ala Phe Leu Leu Val Arg Lys Leu Pro
                   20
                                        25
Pro Leu Cys His Gly Leu Pro Thr Gln Arg Glu Asp Gly Asn Pro Cys
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<221> SIGNAL <222> -17..-1

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. 515
                35
                                   40
Asp Phe Asp Trp Arg Glu Val Glu Ile Leu Met Phe Leu Ser Ala Ile
Val Met Met Lys Asn Arg Arg Ser Ile Thr Val Glu Gln His Ile Gly
                           70
Asn Ile Phe Met Phe Ser Lys Val Ala Asn Thr Ile Leu Phe Phe Arq
                       85
Leu Asp Ile Arg Met Gly Leu Leu Tyr Ile Thr Leu Cys Ile Val Phe
                   100
                                       105
Leu Met Thr Cys Lys Pro Pro Leu Tyr Met Gly Pro Glu Tyr Ile Xaa
               115
                                   120
Tyr Phe Asn Asp Lys Thr Ile Asp Glu Glu Leu Glu Arg Asp Lys Arg
                               135
Val Thr Trp Ile Val Glu Phe Phe Ala Xaa Trp Ser Asn Asp Cys Gln
                           150
Ser Phe Ala Pro Ile Tyr Ala Asp Leu Ser Leu Lys Tyr Asn Cys Thr
                       165
Gly Leu Asn Phe Gly Lys Val Asp Val Gly Arg Tyr Thr Asp Val Ser
                   180
                                       185
Thr Arg Tyr Lys Val Ser Thr Ser Pro Leu Thr Lys Gln Leu Pro Thr
              195
                                  200
Leu Ile Leu Phe Gln Gly Gly Lys Glu Ala Met Arg Arg Pro Gln
                               215
<210> 1075
<211> 153
<212> PRT
<213> Homo sapiens
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<221> SIGNAL
<222> -17..-1
<400> 1075
Met Thr Met Tyr Leu Trp Leu Lys Leu Leu Ala Phe Gly Phe Ala Phe
    -15
                       -10
Leu Asp Thr Glu Val Phe Val Thr Gly Gln Ser Pro Thr Pro Ser Pro
Thr Gly Leu Thr Thr Ala Lys Met Pro Ser Val Pro Leu Ser Ser Asp
               20
                                   25
Pro Leu Pro Thr His Thr Thr Ala Phe Ser Pro Ala Ser Thr Phe Glu
                               40
Arg Glu Asn Asp Phe Ser Glu Thr Thr Thr Ser Leu Ser Pro Asp Asn
                           55
Thr Ser Thr Gln Val Ser Pro Asp Ser Leu Asp Asn Ala Ser Ala Phe
                       70
Xaa Thr Thr Gly Val Ser Ser Val Gln Thr Pro Xaa Leu Pro Thr His
                                       90
                   85
Ala Asp Ser Gln Thr Pro Ser Ala Gly Thr Asp Thr Gln Thr Phe Ser
              100
                                  105
Gly Ser Ala Xaa Met Gln Asn Ser Thr Leu Pro Gln Ala Ala Met Leu
          115
                              120
Ser Gln Met Ser Gln Glu Arg Gly Val
   130
<210> 1076
<211> 42
<212> PRT
<213> Homo sapiens
<220>
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<400> 1076
Met Thr Met Tyr Leu Trp Leu Lys Leu Leu Ala Phe Gly Phe Ala Phe
                     -10
       -15
Leu Asp Thr Glu Val Phe Val Thr Gly Gln Ser Pro Thr Pro Ser Pro
Thr Gly Val Ser Ser Val Gln Thr Pro Gln
                20
<210> 1077
<211> 87
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -17..-1
<400> 1077
Met Thr Met Tyr Leu Trp Leu Lys Leu Leu Ala Phe Gly Phe Ala Phe
      -15
                           -10
                                                -5
Leu Asp Thr Glu Val Phe Val Thr Gly Gln Ser Pro Thr Pro Ser Pro
  1
                                       10
Thr Gly Val Ser Ser Val Gln Thr Pro His Leu Pro Thr His Ala Asp
               20
                                   25
Ser Gln Thr Pro Ser Ala Gly Thr Asp Thr Gln Thr Phe Ser Gly Ser
           35
                               40
Ala Xaa Met Gln Asn Ser Thr Leu Pro Gln Ala Ala Met Leu Ser Gln
Met Ser Gln Glu Arg Gly Val
   65
<210> 1078
<211> 42
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -36..-1
<400> 1078
Met Arg Gly Ala Thr Trp Pro Trp Pro Cys Leu Pro Ala Arg Thr Ser
                       -30
                                           -25
Thr Ala Ala Ser Ile Ala Arg Leu Phe Leu Leu Ser Gly Thr Ile Trp
                   -15
Ile Ala Ile Cys Lys Pro Thr Thr Asn Gly
<210> 1079
<211> 72
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -64...-1
<400> 1079
Met Gly Val Leu Pro Asp Leu Val Val Glu Ile Phe Gly Val Asn Lys
                                   ~55
Cys Arg Leu Ser Trp Gly Leu Val Leu Glu Ser Leu Gln Gln Pro Leu
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-40

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Ile Asn Arg His Leu Ile Tyr Cys Leu Gly Asp Ile Ile Leu Xaa Xaa
       -30
                           -25
                                               -20
Leu Asp Leu Ser Ala Leu Leu Arg Ser Leu Leu Pro Xaa Leu Xaa
Gln Ile Pro Gln Ala Thr Leu Arg
<210> 1080
<211> 42
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -15..-1
<400> 1080
Met Thr Ala Leu Gly Phe Val Leu Leu Ala Pro Arg Gly Trp Gly Ser
                   -10
                                       -5
Leu Thr Val Met Val Glu Gly Lys Glu Glu Gln Val Thr Ser Tyr Thr
        5
Asp Gly Ser Arg Gln Arg Asp Ser Asn Phe
<210> 1081
<211> 64
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -39..-1
<400> 1081
Met Lys Arg Ile Arg Arg Lys Arg Arg Asn Glu Val Thr Ile Gln Pro
               ~35
                    -30
Phe Pro Ile Arg Leu Pro Leu Leu Pro Pro Leu Ile Ser Phe Leu His
                           · -15
           -20
Thr Leu Gln Val Val Cys Ser Val Ile Met Lys Ser Ile Arg Lys Ala
                          · 1
Phe Val Leu Cys Gly Phe Leu Tyr Phe Glu Phe Phe Asp Gln Lys Leu
                   15
<210> 1082
<211> 59
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -22..-1
<400> 1082
Met Leu Pro Leu Leu His Cys Phe Phe Xaa Val Xaa Leu Phe Xaa Xaa
                           -15
Val Xaa Val Xaa Xaa Ala Ala Leu Leu Arg Tyr Asn Xaa Ser Ile Gln
Xaa Gly Arg Ala Gln Xaa Leu Xaa Pro Xaa Ile Pro Xaa Leu Trp Glu
Thr Lys Xaa Gly Arg Leu Leu Glu Pro Arg Asn
           30
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<211> 30
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -21..-1
<400> 1083
Met Val Ser Val Phe Arg Ser Glu Glu Met Cys Leu Ser Gln Leu Phe
                       -15
                                            -10
Leu Gln Val Glu Ala Ala Tyr Cys Cys Val Ala Glu Leu Gly
                   1
<210> 1084
<211> 41
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -28..-1
<400> 1084
Met Ala Ala Leu Arg Ser Thr Leu Thr Trp Thr Glu Val Val Gly Trp
           -25
                            -20
Trp Ser Val Ala Ser Leu Leu Ser Asp Val Ala Ala Trp Trp Pro Pro
  -10
                           -5
His Ser Thr Ser Thr Arg Gly Gly Val
<210> 1085
<211> 47
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -44..-1
<400> 1085
Met Asn Ala Leu Val Asp Gly Lys Arg Leu Xaa Xaa Cys Ile Arg Tyr
               -40
                                   -35
Phe Asp Ser Ile Ser Leu Tyr Ser Lys Ala Ser Leu Ser Cys Cys Leu
           -25
                               -20
                                                   -15
Val Cys Val Phe Thr Cys Ser Leu Leu Ala Phe Phe Ser Pro Cys
       -10
<210> 1086
<211> 84
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -19..-1
<400> 1086
Met Glu Phe Gly Leu Ser Trp Val Phe Leu Val Ala Ile Leu Lys Gly
               -15
                                  -10
Val Gln Cys Glu Leu Gln Val Val Glu Ser Gly Gly Leu Val Gln
Pro Gly Arg Ser Leu Arg Leu Ser Cys Arg Thr Ser Gly Phe Ala Phe
```

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20
    15
                                             25
Asp Asp Tyr Asn Leu Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu
                    35
                                        40
Glu Trp Val Gly Phe Ile Arg Ser Lys Pro Tyr Gly Glu Thr Thr
Tyr Ala Ala Trp
            65
<210> 1087
<211> 19
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -14..-1
<400> 1087
Met Ser Leu Phe Xaa Leu Xaa Xaa Leu Arg Gln Ser Phe Thr Xaa Xaa
Ala Gln Ala
<210> 1088
<211> 30
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -19..-1
<400> 1088
Met Ile Ser Ala His Cys Ser Phe Tyr Phe Leu Ala Ser Ser Ser Leu
                                    -10
Ser Thr Ser Ala Ser Xaa Arg Thr Gly Ile Thr Asp Val Ser
<210> 1089
<211> 43
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -24..-1
<400> 1089
Met Asn Ala Glu Asn Asn Phe Phe Gly Phe Val Cys Leu Phe Val Phe
               -20
                                    -15
Leu Tyr Thr Thr Pro Cys Asn Cys Phe Gly Leu Glu His Leu Trp Ile
           -5
Leu Ser Phe Met Val Val Leu Gly Xaa Thr Arg
   10 -
<210> 1090
<211> 31
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -23..-1
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<400> 1090
 Met Thr Met Ala Val Gly Ala Ala Xaa Xaa Leu Pro Cys Cys His
             -20
                                 -15
                                                     -10
 Leu Leu Thr Cys Val Ser Ser Leu Arg Xaa Asp Ile Tyr Pro His
 <210> 1091
 <211> 34
 <212> PRT
 <213> Homo sapiens
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 <221> SIGNAL
 <222> -25..-1
 <400> 1091
 Met Arg Arg Lys Arg Arg Glu Arg Lys Glu Arg Lys Ser Ile Leu Leu
                 -20
                                         -15
 Ala Ala Leu Ser Arg Asn Ile Ser Pro Gly Gln Thr Tyr Arg Thr Ser
                - 5
 Pro Ala
 <210> 1092
 <211> 30
 <212> PRT
 <213> Homo sapiens
 <220>
 <221> SIGNAL
 <222> -23..-1
 <400> 1092
 Met Gly Ser Pro Tyr Val Ala His Val Gly Leu Glu Leu Leu Thr Ser
           -20
                                -15
 Ser Asp Pro Pro Ser Leu Ala Ser Gln Val Leu Gly Ile His
       -5
                             1
 <210> 1093
 <211> 45
 <212> PRT
 <213> Homo sapiens
 <220>
 <221> SIGNAL
 <222> -19..-1
 <400> 1093
 Met His Leu Tyr Thr His Val Cys Trp Leu Thr Leu Thr Leu Ala His
                -15
                                    -10
 Ser His Ser Leu Thr His Thr His Thr Leu Thr Pro Ser His Thr Arq
 Thr His Ser His Thr Cys Ala Cys Leu His Ala His Lys
  15
                        20
 <210> 1094
 <211> 51
 <212> PRT
 <213> Homo sapiens
 <220>
 <221> SIGNAL
<222> -15..-1
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<400> 1094
Met Arg Leu Ser Leu Thr Phe Tyr His Phe Pro Leu Cys Trp Gly His
                    -10
                                        - 5
Gln Ala Val Pro Thr Trp Trp Xaa Xaa Ile Ile Gln Pro Cys His Cys
                                10
Ala Leu Cys Thr Ser Ala Glu Gly Val Gln Ser His Ile Ile Ser Xaa
     20
                            25
Ile Tyr Arg
   35
<210> 1095
<211> 80
<212> PRT
<213> Homo sapiens
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<221> SIGNAL
<222> -14..-1
<400> 1095
Met Asn Val Leu Ile Ile Val Phe Val Ala Phe Ala Phe Gly Phe Leu
                -10
                                    -5
Val Met Lys Ser Leu Leu Lys Pro Met Ser Arg Arg Val Phe Leu Met
Leu Ser Ser Arg Ile Phe Met Val Ser Gly Leu Arg Phe Lys Ser Leu
                        25
Ile His Leu Glu Leu Ile Phe Val Tyr Lys Leu Arg Asp Glu Asp Pro
                   40
                                        45
Val Ser Phe Phe Tyr Met Trp Leu Ala Asn Tyr Pro Ser Thr Ile Cys
                                    60
<210> 1096
<211> 116
<212> PRT
<213> Homo sapiens
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<221> SIGNAL
<222> -20..-1
<400> 1096
Met Ser Arg Arg Ser Met Leu Leu Ala Trp Ala Leu Pro Ser Leu Leu
                   -15
                                        -10
Arg Leu Gly Ala Ala Gln Glu Thr Glu Asp Pro Ala Cys Cys Ser Pro
Ile Val Pro Arg Asn Glu Trp Lys Ala Leu Ala Ser Glu Cys Ala Gln
His Leu Ser Leu Pro Leu Arg Tyr Val Val Val Ser His Thr Ala Gly
   30
Ser Ser Cys Asn Thr Xaa Ala Ser Cys Gln Gln Gln Ala Arg Asn Val
Gln His Tyr His Met Lys Thr Leu Gly Trp Cys Asp Val Gly Tyr Asn
                                   70
                                                        75 '
Xaa Leu Asp Trp Arg Arg Ala Arg Ile Xaa Gly Pro Trp Xaa Glu
Leu His Gly Xaa
       95
<210> 1097
<211> 19
<212> PRT
<213> Homo sapiens
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<220> ·
 <221> SIGNAL
 <222> -14..-1
 <400> 1097
 Met Val Phe Leu Phe Leu Met Ile Ser Val Phe Ala Gly Cys Gln Ile
                -10
 Pro Ser Gly
    ·5
 <210> 1098
 <211> 38
 <212> PRT
 <213> Homo sapiens
 <220>
 <221> SIGNAL
 <222> -21..-1
 <400> 1098
 Met Gly Ser Arg Pro Val Ser Xaa Ala Gly Leu Glu Leu Leu Ala Ser
                     -15
                                          -10
 Ser Asn Ser Ser Ala Leu Pro Phe Gln Cys Ser Gly Ile Thr Gly Met
                                  5
           1
 Ser Xaa His Thr Leu Ala
           15
<210> 1099
 <211> 19
 <212> PRT
 <213> Homo sapiens
<220>
 <221> SIGNAL
 <222> -13..-1
<400> 1099
Met Leu Cys His Leu Ser Leu Val Phe Leu Gly Xaa Gly Gln Phe Trp
                               - 5
 Ser Gln Asn
   5
 <210> 1100
 <211> 30
 <212> PRT
 <213> Homo sapiens
 <220>
 <221> SIGNAL
 <222> -17..-1
<400> 1100
Met Thr Asn Leu Phe Met Cys Leu Phe Ala Ile Cys Ile Ser Ser Asn
    -15
                    -10
                                               -5
Ala Lys Cys Leu Phe Ser Leu Phe Pro Phe Phe Ile Glu Gly
                 . 5
<210> 1101
<211> 48
<212> PRT
.<213> Homo sapiens
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<220>
<221> SIGNAL
<222> -27..-1
<400> 1101
Met Leu Gly Tyr Ile Trp Xaa Gln Asp Lys Val Phe Ala Asn Cys Val
                            -20
Leu Phe Thr Leu Leu Val Ser Thr Arg Ser Gly Arg Ser Arg Ala Gly
                       ~5
Cys Ala Trp Arg Trp Arg Gly Arg Trp Ser Val Gly Gln Lys Gly Xaa
                                   15
<210> 1102
<211> 28
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -15..-1
<400> 1102
Met Xaa Leu Ile Leu Ser Leu Gln Val Cys Arg Pro Ala Thr Leu Asp
-15 -10
Gln Ala Thr Arg Ala Thr Thr Pro Cys Arg Leu Arg
<210> 1103
<211> 41
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -37..-1
<400> 1103
Met Cys His Arg Arg Trp Leu His Leu Ser Thr Arg His Leu Gly Phe
       -35
                           -30
Lys Pro Arg Ile His Tyr Val Phe Val Leu Met Leu Ser Leu Pro Leu
                       -15
Pro Pro Thr Pro Gln Gln Ala Leu Gly
<210> 1104
<211> 36
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -19..-1
<400> 1104
Met Asp His Val Val Ile Phe Val Ile Phe Pro Ala Ala Leu Leu Leu
             -15
                                  -10
Cys Trp Gly Gly Leu Ile Pro Leu Cys Ile Ile Tyr Pro Pro Ile Ala
                           5.
Asp Thr Val Gly
  15
<210> 1105
<211> 30
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<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -25..-1
<400> 1105
Met Leu Thr Asn Leu Phe Phe Gln Val Ala His Pro Leu Ile Ile Ile
                    -20
                                         -15
Leu Xaa Phe Asp Ile Tyr Ser Leu Ala Phe Ile His Asp Val
                -5
                                     1
<210> 1106
<211> 27
<212> PRT
<213> Homo sapiens
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<221> SIGNAL
<222> -14..-1
<400> 1106
Met Leu Phe Gly Leu Arg Gly Met Leu Pro Leu Thr Gln Gln Ala Pro
                -10
Ile Pro His Leu Arg Cys Lys Leu Ser Val Thr
                            10
<210> 1107
<211> 79
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -21..-1
<400> 1107
Met Arg Val Cys Met Arg Leu Cys Ala Cys Val Tyr Ala Cys Val Cys
   -20
                        -15
                                            -10
Ala Ser Val Ser Ala Cys Val Tyr Xaa Cys Val Cys Met Xaa Val Arg
-5
Ala His Leu Cys Val Cys Met Cys Val Cys Met Cys Val His Leu Cys
                                20
Val Cys Met Cys Val Cys Val Cys Ala Ser Val Cys Val Cys Met Cys
                            35
Ala Cys Val Cys Met Cys Val Cys Val Arg Ala Ser Val Cys Val
<210> 1108
<211> 23
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -21..-1
<400> 1108
Met Val Ile Thr Ser Asn Ser Tyr Leu Ile Ala Asn Leu Val Leu Phe
Ile Ser Ile Ala Ala Leu Arg
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<210> 1109
<211> 57
 <212> PRT
 <213> Homo sapiens
<220>
 <221> SIGNAL
 <222> -51..-1
<400> 1109
Met Glu Glu Leu Asp Arg Lys Trp Arg Glu Lys Val Leu Pro Ala Ala
    -50
                         -45
                                             -40
Lys Leu Ile Lys Arg Arg Asn Leu Phe Ser Thr Cys Thr Pro Gln Tyr
-35
                    -30
                                         -25
Gly Thr His Ala Ala Phe Leu Ser Leu His Ala Ser Leu Val Thr Lys
                -15
                                    -10
                                                         - 5
Ala Phe Ser Ile Asn Ser Trp Glu Trp
                            5
            1
<210> 1110
<211> 27
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -25..-1
<400> 1110
Met Val Ser Gly Ala Gln Ala Pro Ser Ser Gln Arg Pro Leu Leu Leu
                    -20
                                        -15
Cys Pro Leu Ser Ser Gly Ser Pro Cys Pro Arg
                 -5
<210> 1111
<211> 32
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -27..-1
<400> 1111
Met Ser Cys Leu Leu Arg Ala Tyr Ile Ile Trp Ile Phe Pro Ser Phe
     -25
                            -20
                                                -15
Leu Pro Ser Leu Leu Ser Ser Phe Leu Leu Ser Leu Pro Pro Ser Gly
<210> 1112
<211> 67
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -36..-1
<400> 1112
Met Phe Gln Leu Leu Ile Leu Cys Gln Met Asn Ser Leu Lys Ile Phe
                        ~30
Ser Pro Ile Leu Gly Trp Ser Leu His Phe Val Tyr Cys Phe Leu Cys
```

```
-15
                                       -10
Cys Ala Glu Ala Phe Leu Leu Asp Met Ile Pro Phe Met Gln Phe Tyr
               1
                               5
Phe Gly Tyr Leu Cys Leu Trp Gly Ile Thr Leu Lys Ile Phe Ala Gln
      15
Ser Asn Trp
   30 ·
<210> 1113
<211> 54
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -48..-1
<400> 1113
Met Ala Leu Leu Gly Lys Arg Cys Asp Val Pro Thr Asn Gly Cys Gly
           -45
                              -40
Pro Asp Arg Xaa Xaa Gly Xaa Asn Pro Gln Xaa Arg Asp His His
                          -25
                                               -20
Gln Xaa Xaa Val Cys Leu Arg Leu His Val Leu Ser Ala Val Gln Thr
Glu Arg Arg Gly Asp Gly
               5
<210> 1114
<211> 37
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -32..-1
<400> 1114
Met Arg Pro Ala Leu Arg Ser Phe Trp His Ser Ser Gly Gly Pro Pro
              -25
                                               -20
Pro Ser Ala Thr Leu Ala Leu Leu Ser Ser Asp Ser Val Ala Thr Gly
Ser Val Val Ser Arg
<210> 1115
<211> 49
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -26..-1
<400> 1115
Met Leu Cys Ala Cys Lys Ala Arg Gly Val Met Leu Leu Leu Phe Ser
                        -20
                                           -15
Gly Trp Leu Val Trp Trp Gly Ser Arg Ser Ser Gln Xaa Leu Arg Met
                   -5
                                       1
Pro Glu Xaa Xaa Val Ser Gly Glu Gly Arg Ser Asp Xaa Xaa Pro His
                               15
Gly
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<210> 1116

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<211> 51
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -42..-1
<400> 1116.
Met Ile Ser Ser Ser Leu Ser Gly Arg Val Pro Val Ile Leu Gly Asn
                          -35
Leu Met Gly Val Gly Ala Ala Val Arg Arg Met Gly Phe Ser Leu Ile
 -25
                   -20
                                         -15
Leu Pro Thr Ser Pro Ser Pro Ala His Ser Gly Ser Ala Pro Ser Ala
-10 -5
                                     1
Gly Pro Arg
<210> 1117
<211> 56
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -46..-1
<400> 1117
Met Gly Ile Ile Gln Xaa Ile Leu Ala Thr Ser Arg Asp Cys Tyr Ser
                   -40
Phe Lys Lys Pro Ile Pro Lys Lys Pro Thr Met Leu Ala Leu Ala
-30 · -25
                       -20
Lys Ile Leu Leu Ile Ser Thr Leu Phe Tyr Ser Leu Leu Ser Gly Ser
       -10
                                  - 5
His Gly Lys Xaa Asn Gln Asp Val
<210> 1118
<211> 29
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -23..-1
<400> 1118
Met Met Leu Ser Thr Phe Ser Tyr Ala Cys Leu Pro Phe Val Cys Leu
                           -15
         -20
Leu Leu Arg Asn Val Tyr Ser Asp Leu Leu Pro Asn Arg
<210> 1119
<211> 30
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -24..-1
Met Leu Ala Ile Leu Thr Gly Gly Arg Trp Tyr Leu Ile Val Val Leu
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Val Cys Ile Ser Leu Val Ile Ile Asp Asp Asp Glu His Gly
                                1
<210> 1120
<211> 18
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -14..-1
<400> 1120
Met Leu Leu Pro Leu Gly Leu Lys Val Leu Gly Leu Gln Ala Arg Gly
               -10
                                    -5
Thr Thr
<210> 1121
<211> 48
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -28..-1
<400> 1121
Met Arg Pro Thr Met Glu Phe His Ser Val Leu Cys Gly Val Thr Pro
           -25
                               -20
Thr Leu Leu Val Met Trp Leu Ser Pro Gln Met Ala Ser Ser Pro Ser
 -10
                          -5
Gln Ala Pro Gly Met Glu Pro Cys Ala Ser Gly Ile Ser Gln Arg Ala
                   10
                                        15
<210> 1122
<211> 52
<212> PRT
<213> Homo sapiens
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<222> -33..-1
<400> 1122
Met Gly Lys Lys Ile Trp Thr Pro Ser Ser Tyr Pro Met Pro Ser
           -30
His Lys His Val Ser Leu Cys Leu Leu Thr Val Ala Val Leu Val Leu
                           -10
Thr Phe Lys Ser Leu Ile His Phe Glu Xaa Ile Phe Ala Tyr Glu Ile
Gly Val Gln Gly
<210> 1123
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<212> PRT
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<222> -24..-1
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Met Ser Pro Val Leu Cys Phe His Arg Cys Ser Cys Pro Ser Leu Leu

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-20
                                   -15
Ser Pro Ile Ser Pro Ser Gln Ala Cys Pro Glu Pro Leu Leu Gly
                               1
<210> 1124
<211> 34
<212> PRT
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<222> -24..-1
<400> 1124
Met Leu Gln Leu Ser Phe Ser Val Phe Ile Leu Ile Met Phe Val Cys
         -20
                              -15
Met Cys Val Cys Val Cys Val Tyr Arg Leu Phe Ser Ser Ser
                               1
Ser Pro
  10
<210> 1125
<211> 101
<212> PRT
<213> Homo sapiens
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<222> -91..-1
<400> 1125
Met Lys Ser Thr Val Ser Ser Arg Glu Val Ala Thr Val Asp Lys Met
                       -85
Lys Arg Arg His Ala Glu Tyr Cys Ala Gln Gly Leu Gln Arg Phe Lys
                   -70
                                      -65
Ala Gln Leu Ser Gln Asp Thr Leu Pro Xaa His Pro His Leu Glu Xaa
               -55
                                  -50
Glu Lys Gly Leu Glu Gly Leu Glu Glu Asn Val Pro Leu Lys Gly Glu
                              -35
Lys Pro Gly Glu Gly Pro Glu Ser Pro Lys Lys Arg Arg Arg Val
                          -20
                                           -15
Leu Leu Gly Ala Gly Ile Pro Pro Val Ser Ser Ala Pro Arg Arg Gln
  -10
                                          1
Ser Gln Gln Ala Thr
               10
<210> 1126
<211> 36
<212> PRT
<213> Homo sapiens
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<221> SIGNAL
<222> -20..-1
<400> 1126
Met His Asn Ser Cys Arg Pro Val His Leu Phe Phe Phe Phe Xaa
                -15
                                     -10.
Glu Thr Gly Ser Arg Ser Asn Xaa Trp Leu Glu Xaa Ser Gly Ala Ile
Ile Ala Asn Ser
       15
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<210> 1127
<211> 44
<212> PRT
<213> Homo sapiens
<220>
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<222> -42..-1
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Met Glu Ala Tyr Leu Asn Asp Ser Leu Leu Thr Pro Ser Asp Ser Pro
       -40
                           -35
                                               -30
Asp Phe Glu Ser Val Gln Ala Gly Pro Xaa Ala Arg Pro Thr Phe Arg
                       -20
                                            -15
Leu Tyr Leu Ser Leu Pro Val Ser Gln Ala Gly Pro
<210> 1128
<211> 70
<212> PRT
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<221> SIGNAL
<222> -14..-1
<400> 1128
Met Pro Ala Leu Gly Pro Ala Leu Leu Gln Gly Ser Leu Xaa Arg Val
            -10
                                   -5
Gly Pro His Pro Pro Ala Pro Ser Thr Asn Cys Ile His Ser Gln Trp
. 5
                           10
His Val Ser Ala Ala Xaa Gly Lys Gly Pro His Leu Arg His Pro Leu
                       25
                                           30
Xaa Gly Xaa Tyr Gln Leu Pro Val Pro Ala Glu Pro Trp Ala Ala Ala
           . 40
Gly Gly His Ser Val His
               55
<210> 1129
<211> 21
<212> PRT
<213> Homo sapiens
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<222> -19..-1
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Met Val Gly Ile Leu Pro Leu Cys Cys Ser Gly Cys Val Pro Ser Leu
               -15
Cys Cys Ser Ser Tyr
<210> 1130
<211> 22
<212> PRT
<213> Homo sapiens
<220>
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<222> -14..-1
<400> 1130
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WO 99/53051 531 Met Ala His Ser Ile Leu Leu Leu Ala Ser Gln Ala Gly Cys Leu Arg -10 Ser Phe Leu Gly Asn Trp 5 <210> 1131 <211> 30 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -20..-1 <400> 1131 Met Thr Glu Phe Gly Leu Ser Trp Val Phe Leu Val Ala Ile Phe Lys -15 -10 Gly Val His Cys Glu Gly Xaa Ile Gly Gly Val Gly Gly Ala 1 <210> 1132 <211> 16 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -14..-1 <400> 1132 Met Asn Thr Val Phe Leu Leu Phe Phe Gly Cys Phe Phe Phe Glu <210> 1133 <211> 47 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -24..-1 <400> 1133 Met Trp Ala Ser Ser Pro Trp Pro Ser Ala Trp Ser Cys Cys Leu -20 -15 Ser Ser Ser Phe Ile Ala Gly Arg Arg Gly Trp Thr Gln Met Trp Leu Thr Arg Pro Phe Ser Pro Gln Ala Ser Ser Pro Ser Ala 10 <210> 1134 <211> 49 <212> PRT <213> Homo sapiens <220>

<221> SIGNAL <222> -33..-1

<400> 1134 Met Thr Met Pro Ile Ser Ser Tyr Ser Gln Asn Val Leu Ser Asn Phe -30 -25

His Asp Gly Tyr Phe Met Leu Ile Ile Leu Ser Ala Ile Leu Leu Asn

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-10
       -15
                                               -5
Ser Phe Ile Gly Cys Val Ser Phe Tyr His Cys Phe Ser Trp Gly Ser
               5
                                    10
Gly
<210> 1135
<211> 28
<212> PRT
<213> Homo sapiens
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<221> SIGNAL
<222> -20..-1
<400> 1135
Met Leu Thr His Gly Ala Ser Leu Ser Leu Val Ile Phe Leu Leu Thr
                   -15
Val Lys His Cys Phe Arg Tyr Arg Val Tyr Lys Thr
               1
<210> 1136
<211> 35
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -22..-1
<400> 1136
Met Ser Ser Val Glu Thr Asp Trp Gly Phe Trp Thr Ser Ile Pro Ile
                          -15
Leu Pro Leu Ser Ser Gly Arg Gln Leu Pro Leu Pro Thr Arg Glu Trp
 -5
Gly Met Trp
<210> 1137
<211> 82
<212> PRT
<213> Homo sapiens
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<221> SIGNAL
<222> -33..-1
<400> 1137
Met Phe Ala Ser Pro Arg Arg Trp Ser Ser Xaa Lys Ala Phe Ser Gly
        -30
                               -25
Gln Arg Thr Leu Leu Ser Ala Ile Leu Ser Met Leu Ser Leu Ser Phe
      -15
                           -10
Ser Thr Thr Ser Leu Leu Ser Asn Tyr Trp Phe Val Gly Thr Gln Lys
 . 1
                  5
                                       10
Val Pro Lys Pro Leu Cys Glu Lys Gly Leu Ala Ala Lys Cys Phe Asp
               20
                                   25
Met Pro Val Ser Leu Asp Gly Asp Thr Asn Thr Ser Thr Gln Glu Val
                               40
Val Xaa
<210> 1138
<211> 63
<212> PRT
<213> Homo sapiens
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<222> -16..-1
<400> 1138
Met Pro Ile His Ser Val Phe Leu Cys Ala Pro Ala Leu Val Phe Pro
                        -10
   -15
                                          . -5
Arg Pro Val Ala Trp Lys Ala Glu Arg Pro Ser Leu Cys Phe Gly Ala
               5
                                   10
Ser Leu Pro Pro Leu Gly Arg Ser Leu Leu Gly Gln Gly Ser Ser Phe
    · 20
                               25
Ile Ser Trp Gly Thr Gln Ala Ala Ile Val Glu Leu Xaa Pro His
                            40
<210> 1139
<211> 80
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -62..-1
<400> 1139
Met Val Tyr Asp Glu Lys Ser Leu Ser Cys Ser His Thr Pro Ala Thr
       -60
                            -55
                                                -50
Gln Phe Leu Ser Trp Asp Ala Ser Ser Val Tyr Ser Phe Leu Tyr Ile
                       -40
                                            -35
Leu Ser Ala Arg Val Asn Val Asp Val Xaa Xaa Tyr Ile Arg Val Tyr
                   -25
                                       -20
Ile Leu Ala Cys Val Phe Phe Leu Ser His Pro Leu Phe Xaa Xaa Pro
               -10
                                   -5
Asn Gly Ser Val Tyr Cys Xaa Arg His Ser Pro Pro Tyr Leu Phe Cys
                          10
<210> 1140
<211> 38
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -36..-1
<400> 1140
Met Leu Pro Leu Ser Pro Thr Lys Phe Leu Asn Val Phe Leu Gly Leu
                       -30
Phe Leu Tyr Tyr Leu Gln Leu Val Cys Leu Leu Ile Ile Ser Leu Val
Leu Ile.Ser Gly Leu Gly
<210> 1141
<211> 48
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -29..-1
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Met Asp Lys Val Glu Leu Pro Pro Pro Asp Leu Gly Pro Ser Ser Ala

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-25
                                     -20
Leu Asn Gln Thr Leu Met Leu Leu Arg Glu Val Leu Ala Ser His Asp
            -10
                                -5
Ser Ser Val Val Pro Leu Asp Ala Arg Gln Ala Asp Phe Val Gln Gly
  5
                        10 '
                                             15
<210> 1142
<211> 61
<212> PRT
<213> Homo sapiens
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<221> SIGNAL
<222> -32..-1
<400> 1142
Met Gly Gly Thr Ala Gly Trp Ser Ser Gln Asn Thr His Asn Ile Xaa
        -30
                            -25
Val His His Leu Val Trp Leu Trp Phe Val Val Pro Gln Thr Ile Thr
                        -10
                                            -5
Met Ile Thr Pro Lys Ile Thr Glu His Arg Pro Xaa Ile Thr Asp Xaa
Xaa Ile Met Xaa Thr Phe Glu Xaa Leu Gly Glu Leu Pro
<210> 1143
<211> 30
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -18..-1
<400> 1143
Met Cys Leu Ser Val Ala Leu Tyr Leu Cys Val Cys Val Cys
           -15
                                -10
Leu Ile Ala Arg Val Tyr Phe Cys Ile Tyr Val Cys Val Trp
                        5
<210> 1144
<211> 29
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -14..-1
<400> 1144
Met Leu His Leu Leu Phe Gly Leu Phe Pro Val Leu Trp Met Phe Leu
               -10
                                    -5
Val Tyr Phe Phe Leu Ser Ser Phe Phe Phe Phe Phe
                            10
<210> 1145
<211> 22
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -18..-1
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<400> 1145
Met Tyr Val Cys Xaa Cys Val Tyr Leu Phe Cys Ala Cys Met Cys Val
        -15
                             -10
Cys Ala Phe Phe Phe
   1
<210> 1146
<211> 55
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -36..-1
<400> 1146
Met Lys Xaa Asn Asn Leu Arg Arg Gln Ser Pro Ala Leu Arg His Cys
                      -30
                                      -25
Trp Arg Xaa Glu Thr Asp Phe Phe Leu Phe Thr Leu Ile Gly Ala Ser
                -15
                        -10
Leu Leu Gln Ser Ala Ser Gly Pro Cys Arg Ile Ser Xaa Xaa Leu Lys
              1
                         . 5
Trp His Ser Lys Gly Thr Leu
      15
<210> 1147
<211> 54
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -20..-1
<400> 1147
Met Trp Pro Lys Xaa Gly Leu Leu Gly Leu Gly Leu Pro Leu Leu Pro
                -15
                                   -10
Pro Asn His Pro Ser Val Ala Gln Gly Thr Leu Val Ser Ser His Ser
              1
Gly Ser Gly Ser Glu Gly Arg Val Ala Leu Arg Ser Asp Val His Ser
      15
                          20
Pro Lys Thr Thr Xaa Gln
  30
<210> 1148
<211> 135
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -42..-1
<400> 1148
Met Tyr Leu Ile Arg Glu Ser His Ala Ser Gly Ser Ser Ser Val Thr
                                  -30
                         -35
Ser Ser Cys Ser Leu Xaa Ser Xaa Ser Pro Asn Pro Gln Ala Met Ala
                      -20
                                        -15
Xaa Leu Phe Leu Ser Ala Pro Pro Gln Ala Glu Val Thr Phe Glu Asp
-10 -5
                                     1
Val Ala Val Tyr Leu Ser Arg Glu Glu Trp Gly Arg Leu Gly Pro Ala
          10
                             15
```

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Gln Arg Gly Xaa Tyr Arg Asp Val Met Leu Glu Thr Tyr Xaa Asn Xaa
                              30
 Val Ser Leu Gly Val Gly Pro Ala Gly Pro Lys Xaa Gly Val Ile Ser
                          45
 Gln Leu Glu Arg Gly Asp Glu Pro Trp Val Leu Asp Val Gln Gly Thr
                      60
 Ser Gly Lys Glu His Leu Lys Lys Ser Thr Ala Gln Leu Leu Gly Pro
                 75
 Glu Leu Lys Tyr Lys Glu Leu
              90
 <210> 1149
 <211> 55
 <212> PRT
 <213> Homo sapiens
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 <221> SIGNAL
 <222> -37..-1
 <400> 1149
 Met Ile Pro Arg Arg Thr Ser Ala Ser Arg Ala Pro Ser Val Pro Gln
         -35
                             -30
 Asn Ala Gly Leu Ser Pro Leu Pro Ala Leu Ser Ser Leu Cys Val Ser
                         . -15
                                              -10
 Trp Gly Thr Ser Ser Thr Val Thr Arg Leu Arg Pro Trp Ile Ser Pro
                                     5
 Thr Trp Thr Ser Arg Ala Arg
             15
 <210> 1150
 <211> 56
 <212> PRT
 <213> Homo sapiens
 <220>
. <221> SIGNAL
 <222> -14..-1
 <400> 1150
 Met Val Cys Ile Phe Cys Phe Leu Thr Ser Lys Ala Phe Pro Asn Pro
                 -10
                                     -5
 Arg Ser Gln Asp Phe Leu Leu Asp Phe Ser Arg His Xaa Ile Gly Leu
                             10
 Gly Phe Thr Phe Arg Ser Ala Met His Phe Glu Asn Phe Arg Leu Xaa
 Gly Leu Gly Gln Asp Ser Leu Cys
 <210> 1151
 <211> 25
 <212> PRT
 <213> Homo sapiens
 <220>
 <221> SIGNAL
 <222> -20..-1
 <400> 1151
 Met Xaa Xaa Tyr Xaa Xaa Xaa Gly Phe Cys Ser Val Thr Ser Ser Pro
 -20
                  -15
 Leu Ala Ser Ala Gly Arg Thr Thr Arg
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<210> 1152
<211> 38
<212> PRT
<213> Homo sapiens
<220>.
<221> SIGNAL
<222> -23..-1
<400> 1152
Met Ser Leu Xaa Xaa Leu Cys Asp Pro Asp Leu Val Pro Cys Pro Leu
           -20
                                -15
Leu Ile Ser Val Ala Leu Ser Val Lys Phe His Ile Xaa Gln Gln Val
       -5
                            1
Asn Leu Pro Cys Ser Ser
10
<210> 1153
<211> 80
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -39..-1
<400> 1153
Met Met Ile Leu Ile Leu Glu His Ile Val Thr Xaa Lys Arg
                                    -30
Asn Pro Lys Pro Val Thr Val Pro Ala Phe Leu Xaa Pro Cys Leu Thr
            -20
                                -15
Ser Phe Ser Cys Xaa Gly Ala Ser Phe Ser Leu Xaa Gly Xaa Arg Arg
                            1
Gly Trp Gln His Gly Ser Cys Cys Ser Thr Ile Pro Leu Phe Xaa Thr
                   15
                                        20
Leu Asn Ser Leu Gly Gln Gly Leu Ile Gly Pro Ala Tyr Ile Gly Ala
<210> 1154
<211> 19
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -16..-1
<400> 1154
Met Ser Thr His Ala Ile Ser Ile Leu Leu Cys Ile Gly Ala Ser Ser
   -15
                        -10
Gln Gly Arg
<210> 1155
<211> 67
<212> PRT
<213> Homo sapiens -
<220>
<221> SIGNAL
<222> -31..-1
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<400> 1155
Met Glu Glu Gln Glu Thr Glu Glu Val Gly Gly Arg Ser Ser Arg Lys
Asn Ala Ala Thr Val Asn Ala Ala Ser Leu Pro Pro Cys Phe Gly Val
                    -10
                                         -5
Lys Ser Cys Arg Cys Arg Cys Ser Cys Arg Arg Cys Leu Leu Tyr
                                10
Phe Ser Trp Pro Arg Gly Arg Ile Ser Pro Pro Val Gly Gln Cys Ala
        20
                            25
Gly Arg Gly
    35
<210> 1156
<211> 145
<212> PRT
<213> Homo sapiens
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<221> SIGNAL
<222> -33..-1
<400> 1156
Met Arg Gly Ile Gln Ala Lys Gly Ser Pro Gly Gln Ser Ser Ala Xaa
                            -25
Val Leu Xaa Pro Cys Cys Cys His Ala Gly Ala Ser Ser Gly Ala Thr
                            -10
Ala Trp Glu Glu Thr Pro Arg Ser Arg Cys His Ile Ala Val Xaa Ser
Thr Asn Thr Ala Ser Arg Gly Arg Thr Trp Cys Arg Ala Thr Gly Pro
                20
                                    25
Cys Pro Ser Gly Pro Thr Arg Gly Val Ser Arg Ser Arg Gly Leu Gly
                                40
Ala Gly Phe Leu Ser Pro Phe Cys Cys Leu Phe Ala Phe His Pro Arg
                            55
Leu Pro Trp Cys Ala Glu Val Pro Val Pro Ala Ala Ala His His Met
                        70
Arg Cys Gly Gly Asp Leu Leu Ala Ala Pro Pro Pro Gly Pro Ser Trp
                    85
Phe Ala Arg Phe Pro Pro Leu Val Pro Glu Ser Phe Pro His His Ser
                100
Val
<210> 1157
<211> 34
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -24..-1
<400> 1157
Met Phe Ser Ser Arg Ser Phe Met Val Ser Gly Leu Ile Trp Val Phe
                -20
Gly Leu Val Ser Val Leu Ser Xaa Phe Leu Cys Met Val Tyr Asp Gln
Gly Gln
   10
<210> 1158
<211> 31
<212> PRT
<213> Homo sapiens
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<220>
<221> SIGNAL
<222> -13..-1
<400> 1158
Met Leu Leu Ala Val Ser Leu Ser Leu Val Ser Asn Cys Asn Phe Val '
            -10
                        - 5
Leu Thr Asp Gln Leu Phe Pro Ala Pro Ala Ser Leu Ile Pro Glu
                       10
<210> 1159
<211> 41
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -29..-1
<400> 1159
Met Asn Gln Asp Phe Asn Pro Glu Ile Glu Ala Ser Pro Gln Val Lys
               -25
                                   -20
                                                       ~15
Thr Gly Val Phe Leu Phe Ser Ile Ile Gly Ser Phe Gly Phe Pro Gly
           -10
                               -5
Met Cys Asn Cys Lys Asn Pro Ala Arg
  5
<210> 1160
<211> 24
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -20..-1
<400> 1160
Met Pro Cys Ser Trp Ser His Ile Val Ser Ser Leu Phe Ser Trp Leu
       -15
Leu Ser Leu Thr Ser Val Pro Gly
<210> 1161
<211> 31
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -28..-1
<400> 1161
Met Phe Phe Gly Tyr Ser Glu Asp Ile Tyr Cys Val Ser Gly Pro
           -25
                               -20
Val Leu Ser Cys Cys Cys Leu Thr Ala Gly Arg Ala Arg Leu Trp
    -10
                           -5
<210> 1162
<211> 58
<212> PRT
<213> Homo sapiens
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<220>
<221> SIGNAL
<222> -16..-1
<400> 1162
Met Pro Tyr Ala Ala Leu Ile Cys Pro Trp Ser Ser Gln Val Pro Ser
                     -10
Ser Pro Pro Ala Ser Leu Glu Ala Ser Ser Asn Val Tyr Leu Gln Glu
         5
                                    10
Ser Arg Ala Ala Tyr Ala Ser Val Pro Ala Gly Pro Glu Val Ala Thr
           20
                                25
Gln His Thr Ser Ser Pro Val Thr Pro Met
       35
<210> 1163
<211> 20
<212> PRT
<213> Homo sapiens
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<221> SIGNAL
<222> -18..-1
<400> 1163
Met Gln Leu Leu Tyr Leu Thr Tyr Ser Leu Ala Phe Leu Leu Phe Ile
           -15
                                -10
Lys Ala Gly Thr
       1
<210> 1164
<211> 24
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -20..-1
<400> 1164
Met Ala Pro Ser Arg Pro Arg Ala Ala Ala Val Thr Ser Ser Ala Ala
                    -15
Pro Ser Arg Ala Arg Gln Gly Ala
                1
<210> 1165
<211> 57
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -42..-1
<400> 1165
Met Leu Ala Ser Ala Pro Arg Leu Asn Ser Ala Asp Arg Pro Met Lys
                            -35
                                                -30
Thr Ser Val Leu Arg Gln Arg Lys Gly Ser Val Arg Lys Gln His Leu
                        -20
                                            -15
Leu Ser Trp Ala Xaa Gln Xaa Gly Arg Xaa Gln Val Val Glu Ile Leu
Gln Ser Glu Lys Gln Thr Xaa Xaa Asp
           10
```

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<210> 1166
<211> 47
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -38..-1
<400> 1166
Met Tyr Pro Leu Gly Arg Gly Glu Gln Gly Pro Ala Ala Pro Lys Ser
                                -30
Trp Leu Leu Pro Thr Thr Leu Ala Leu His Gly Ser Leu Asp Ala
     -20
                            -15
                                               -10
Val Ser Gln Ala Gln Gly Arg Pro Gly His Pro Asp Ala Pro Pro
<210> 1167
<211> 21
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -16..-1
<400> 1167
Met Arg Val Phe Ile Ala Ala Leu Phe Thr Ile Ala Glu Thr Trp Asn
 -15
                        -10
Gln Pro Lys Cys Pro
<210> 1168
<211> 55
<212> .PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -30..-1
<400> 1168
Met Ala Lys Gly Leu Arg Val Asn Leu Gly Glu Leu Val Glu Ser Met
                   -25
                                       -20
Arg Leu Cys Phe Leu Ser Val His Phe Arg Leu Arg Trp Gly Asp Ser
               -10
                                   -5
Cys Pro Ser Ser Pro His Arg Glu Thr Phe Pro Ala Gly Pro Val Asn
    5
                           10
Gly Pro Leu Tyr His Pro Arg
   20
<210> 1169
<211> 87
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -17..-1
<400> 1169
Met Pro Ser Pro Gln Leu Leu Val Leu Phe Gly Ser Gln Thr Gly Thr
```

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Ala Gln Asp Val Ser Glu Arg Leu Gly Arg Glu Ala Arg Gly Arg Arg
Leu Gly Cys Arg Val Gln Ala Leu Asp Ser Tyr Pro Val Val Asn Leu
                20
Ile Asn Glu Pro Leu Val Ile Phe Val Cys Ala Thr Xaa Gly Gln Gly
                                40
Asp Pro Pro Asp Asn Met Lys Asn Phe Trp Arg Phe Ile Phe Arg Lys
                            55
Asn Leu Pro Ser Thr Ala Arg
<210> 1170
<211> 48
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -41..-1
<400> 1170
Met Ser Ser Ile Leu Gly Val Ser Ser Ser Trp Trp Tyr Leu Tyr Tyr
                        -35
Gly Tyr Cys Ile Phe Val Lys Lys Cys Ser Phe Cys Ser Phe Leu Phe
                    -20
                                        -15
Leu Ala Cys Ile Phe Gln Gly Xaa Ser Xaa Xaa Xaa Asn Thr Gln Ser
<210> 1171
<211> 51
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -28..-1
<400> 1171
Met Gly Ser Val Leu Gly Leu Cys Ser Met Ala Ser Trp Ile Pro Cys
                                -20
Leu Cys Gly Ser Ala Pro Cys Leu Leu Cys Arg Cys Cys Pro Ser Gly
     -10
Asn Asn Ser Thr Val Thr Arg Leu Ile Tyr Ala Leu Phe Leu Leu Val
                    10
Gly Val Trp
<210> 1172
<211> 109
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -46..-1
<400> 1172
Met Ser Xaa Xaa Arg Leu Xaa Arg Gln Leu Leu Ser Gln Xaa Arg
                        -40
                                            -35
Xaa Met Thr Cys Glu Asn Glu Ala Gly Ala Gln Cys Gln Lys Ser Ser
                   -25
                                        -20
                                                            -15
Phe Ile Gly Ser Cys Ser Val Met Ser Ser Gly Ala Leu Cys Val Pro
                -10
                                    -5
```

Leu Tyr Tyr Leu Ala Lys Gly Asn Met Cys Ser Ile Cys Gly Met Leu

```
5
                            10
                                                15
Lys Glu Met Asn Gly Leu Trp Ser Glu Cys Asp Ser Leu Lys Asn Thr
                       25
                                           30
Phe Ile Val Trp Xaa Cys Ile Phe Ser Cys Leu Gly Met Gln Leu Xaa
                   40
Ser Ser Xaa Val Ser Asn Val Arg Leu Leu Ser His
<210> 1173
<211> 64
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -26..-1
<400> 1173
Met Pro His Pro Leu Ala Thr Ser Ala Phe Leu Arg Ser Ala Phe Pro
                       -20
                                           -15
Phe Val Cys Leu Thr Phe Cys Val Gly Gly Pro Gly Ile Ser Gly
                   -5
Val Tyr Arg Leu Leu Met Ala Asn Ala Thr Arg Arg Glu Ser Glu Val
           10
                               15
Ser Leu Arg Gly Leu Gly Arg Asp Gly Glu Gly Ala Arg Ala Thr Pro
<210> 1174
<211> 27
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -23..-1
<400> 1174
Met Thr Val Gly Leu His Ile Leu Arg Asp Ser Leu Met Val Phe Leu
          -20
                             -15
Asn Leu Phe Phe Leu Asn Cys Asp Pro His Arg
       -5
<210> 1175
<211> 35
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<222> -21..-1
<400> 1175
Met Val Arq Trp Gly His Pro Pro Met Phe Cys Val Ser Leu Leu Leu
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                                           -10
His His Ala Tyr Pro Leu Pro Ser Thr Met Ile Val Ser Phe Pro Arg
-5
Pro Pro Leu
<210> 1176
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<220>
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<222> -26..-1
<400> 1176
Met Ala Gly Ala Ala Arg Trp Val Gly Gln Xaa Ser Ser Ala Met Val
                        -20
                                            -15
Cys Phe Gly Cys Pro Gly Gly Ala Ser Ser Arg Cys Arg Ser Pro Arg
                    - 5
                                        1
Gly Arg Gln Ala Ser Arg Val Pro Arg Leu Glu Asn Gly Ala Gln Arg
           10
Val Val Arg Thr Met Val His Leu Val Leu Gln Pro Lys Arg Val Thr
                            30
Leu Val His Pro Pro Arg Gly Leu Glu Pro Val Cys Thr Pro Ile Ala
                       45
Xaa Met Xaa Pro Lys Ser His Gly Leu Arg Ser Ser Leu
<210> 1177
<211> 47
<212> PRT
<213> Homo sapiens
<220>
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<222> -34..-1
<400> 1177
Met Gly Val Val Ser Gly Gly Val Gly Asp Leu Thr Thr Lys Thr Gln
                         -25
Glu Asn Gly Leu Leu Pro Xaa Leu Leu Ser Xaa Leu His Gly Leu Leu
                                -10
Tyr Gly Ser Pro Asp Ala Glu Leu Thr Gly Pro Asp Pro Trp Asp
<210> 1178
<211> 17
<212> PRT
<213> Homo sapiens
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<221> SIGNAL
<222> -15..-1
Met Gly Phe Leu Ser Xaa Thr Cys Val Leu Ser Cys Xaa Arg Ser Leu
-15
                    -10
Ser
<210> 1179
<211> 48
<212> PRT
<213> Homo sapiens
<220>
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<222> -39..-1
<400> 1179
Met Glu Tyr Gly Ser Ala Lys Leu Ser Ser Gly Arg Val Phe Tyr Leu
                -35
                                   -30
                                                        -25
Pro Arg Asp Phe Gly Ile Glu Arg Arg Val Leu Val Cys Phe Phe Asn
            -20
                                -15
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Ser Val Ser Phe Leu Phe Gly Val Ser Xaa Lys Lys Ser Xaa Gln Trp
                             1
<210> 1180
 <211> 17
 <212> PRT
 <213> Homo sapiens
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 <221> SIGNAL
<222> -13..-1
 <400> 1180
Met Leu Ser Gly Leu Val Leu Asn Ser Trp Ala Leu Ala Tyr Gln Leu
Ala
<210> 1181
 <211> 23
<212> PRT
 <213> Homo sapiens
<220>
 <221> SIGNAL
 <222> -16..-1
<400> 1181
Met Arg Leu Val Phe Phe Xaa Gly Xaa Ser Ile Ile Leu Val Leu Gly
    -15
Ser Thr Phe Xaa Ala Tyr Leu
<210> 1182
 <211> 35
 <212> PRT
 <213> Homo sapiens
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<221> SIGNAL
 <222> -16..-1
<400> 1182
Met Leu Ser Ser Asp Phe Phe Leu Leu Phe Val Ser Leu Ser Leu Ser
                         -10
                                             -5
Pro Phe Pro Phe Leu Phe Pro Pro Leu Phe Ser Cys Phe Leu Leu
1
                                     10
Pro Thr Arg
<210> 1183
 <211> 58
 <212> PRT
 <213> Homo sapiens
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<221> SIGNAL
<222> -14..-1
<400> 1183
Met Phe Ile Ala Ala Leu Phe Thr Val Ala Lys Ile Trp Asn Gln Pro
                 -10
Lys Cys Pro Ser Thr Asp Glu Trp Ile Asn Lys Met Trp Tyr Ile Tyr
                             10
Thr Met Glu Tyr Tyr Pro Asp Ile Lys Lys Asn Gly Ile Leu Thr Phe
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<220>

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Lys Ala Thr Arg Met Asn Arg Lys Thr Leu
<210> 1184
<211> 31
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<213> Homo sapiens
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<221> SIGNAL
<222> -15..-1
<400> 1184
Met Cys Val Cys Gly Cys Leu Cys Val Trp Met Cys Val Cys Gly Xaa
-15
                   -10
Val Cys Ile Tyr Ile Xaa Val Tyr Val Cys Thr Cys Val Arg Gly
<210> 1185
<211> 61
<212> PRT
<213> Homo sapiens
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<221> SIGNAL
<222> -26..-1
<400> 1185
Met Gly Val Arg Thr Val Cys His Phe Ile Gln Val Phe Leu Ser Leu
  -25
                       -20
                                          -15
Phe Val Phe Phe Trp Leu Val Gly Phe Ser Phe Phe Phe Leu Xaa
                  -5
                                       1
Phe Ser Thr Lys Gln Val Arg Val Glu Gln His Cys Asp Phe Lys Ser
    10
                            15
Thr Pro Xaa Val Glu Ser Ser Ser Thr Val Gly His Ala
                           30
<210> 1186
<211> 63
<212> PRT
<213> Homo sapiens
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<221> SIGNAL
<222> -27..-1
<400> 1186
Met Tyr His Ile Leu Phe Ile His Ser Phe Ile Asp Arg Tyr Leu Ser
                          -20
Cys Phe Tyr Leu Leu Ala Ile Val Ser Asn Ala Val Met Asn Met Gly
Val Gln Met Ser Val Leu Ser Pro Cys Phe Ala Phe Val His Ser Ile
              10
                                  15
Lys Asn Val Lys Val Leu Cys Phe Leu Leu Phe Phe Leu Phe Gly
   . 25
<210> 1187
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<212> PRT
<213> Homo sapiens
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<222> -22..-1
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Met Gln Phe Thr Val Leu Met Cys Pro Val Gln Trp Leu Leu Val Tyr
                   -15
                                               -10
Ser Pro Ser Cys Ala Ala Thr Ile Thr Val Asn Phe Lys Thr Phe Ser
                                       5
                       1
 -5
Ser Pro Gln Thr Gly
<210> 1188
<211> 40
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -37..-1
<400> 1188
Met Arg Arg Ala Trp Thr Gln Glu Arg Glu Pro Arg Pro Cys Glu Pro
                                       -25
                            -30
    -35
Ala Glu Arg Ala Asp Pro Ala Pro Val Ser Cys Leu Ser Ala Gly Leu
                       -15
Arg Val Cys Cys Ser Gln Arg Ser
<210> 1189
<211> 37
<212> PRT ·
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -25..-1
<400> 1189
Met Leu His Leu Ile Cys Ile Ser Leu Ile Val Asn Asp Phe Phe Ile
                                                           -10
                   -20
                                       -15 ·
-25
Cys Leu Leu Ala Ile Cys Val Ser Ser Phe Glu Asn Cys Leu Phe Met
                                                    5
                -5
Ser Leu Ala His Ser.
        10
<210> 1190
 <211> 96
 <212> PRT
 <213> Homo sapiens
 <220>
 <221> SIGNAL
 <222> -63..-1
 <400> 1190
 Met Arg Ser Glu Arg Pro Met Val Trp Cys Cys Leu Phe Val Arg Ser
                                -55
                                                    -50
         -60
 Gln Arg Lys Arg Lys Gln Ser Thr Gln Asp Glu Asp Ala Val Ser Leu
                            -40
                                                -35
 Cys Ser Leu Asp Ile Ser Glu Pro Ser Asn Lys Arg Val Lys Pro Leu
                                            -20
                        -25
 Ser Arg Val Thr Ser Leu Ala Asn Leu Ile Pro Pro Val Lys Ala Xaa
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Pro Leu Lys Arg Phe Ser Gln Thr Leu Gln Arg Ser Ile Ser Phe Arg
                                10
Ser Glu Ser Arg Pro Asp Ile Leu Ala Pro Arg Pro Trp Ser Arg Asn
                             25
<210> 1191
<211> 48
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -20..-1
<400> 1191
Met Val Phe Trp Thr Lys Phe Cys Ile Leu Ile Ser Thr Ala Phe Pro
                    -15
-20
                                        -10
Ser Leu Leu Thr Gln Ile Ile Phe Pro Lys Ser Ile Thr Phe Ala Phe
Gln Phe Phe Trp Asn Arg Glu Lys Gln Lys Thr Lys Thr Pro Thr Gly
    15
                            20
<210> 1192
<211> 65
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -37..-1
<400> 1192
Met Ala Ser Leu Leu Cys Cys Gly Pro Lys Leu Ala Ala Cys Gly Ile
       -35
                            -30
                                                -25
Val Leu Ser Ala Trp Gly Val Ile Met Leu Ile Met Leu Gly Ile Phe
   -20
                        -15
                                            -10
Phe Asn Val His Ser Ala Val Leu Ile Glu Asp Val Pro Phe Thr Glu
Lys Asp Phe Glu Asn Gly Pro Gln Asn Ile Tyr Asn Leu Tyr Glu His
Gly
<210> 1193
<211> 28
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -16..-1
<400> 1193
Met Ser Val Ser Ala Leu Leu Glu Xaa Leu Gln Xaa Ala Ile Pro
                        -10
Arg Xaa Thr Ser Gly Xaa Gln Asp Leu Pro Asn Trp
<210> 1194
<211> 50
<212> PRT
<213> Homo sapiens
<220>
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<221> SIGNAL
<222> -39..-1
<400> 1194
Met Gln Ala Cys Tyr Met Gly Met Trp Tyr Thr Ala Glu Ala Trp Gly
               -35
                                   -30
Thr Ile Glu Ser Leu Thr Gln Val Val Ser Val Ile Ala Ile Val Ser
            -20
                               -15
Phe Thr Thr Leu Cys Ser Ser Leu Tyr Ser Pro Gln Val Val Pro Ser
                            1
Val Gly
10
<210> 1195
<211> 67
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -62..-1
<400> 1195
Met Met Leu Arg Gly Gly Gly Thr Phe Lys Xaa Cys Leu Ser His Glu
                            -55
                                               -50
Gly Ser Ser Phe Thr Lys Gly Leu Ala Gln Glu Cys Val Ser Xaa Ser
                       -40
                                           -35
Cys Gly Thr Arg Leu Ile Thr Ala Val Ala Ser Xaa Tyr Lys Ala Arg
                   -25
                                       -20
Leu Pro Leu Ala Ala Cys Pro Leu Leu Pro Ile Phe Ser His Ala
Arg Ser Ser
       5
<210> 1196
<211> 68
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -40..-1
<400> 1196
Met Ala Lys Asn Pro Pro Glu Asn Cys Glu Asp Cys His Ile Leu Asn
              -35
                                       -30
Ala Glu Ala Phe Lys Ser Lys Lys Ile Cys Lys Ser Leu Lys Ile Cys
               -20
                                   -15
Gly Leu Val Phe Gly Ile Leu Ala Leu Thr Leu Ile Val Leu Phe Trp
           -5
Gly Ser Lys His Phe Trp Pro Glu Val Pro Lys Lys Ala Tyr Asp Met
  10
                       15
Glu His Thr Thr
<210> 1197
<211> 82
<212> PRT
<213> Homo sapiens
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<221> SIGNAL
<222> -41..-1
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<400> 1197
Met Ser Pro Ala Pro Asp Ala Ala Pro Ala Pro Ala Ser Ile Ser Leu
                     -35
                                 -30
Phe Asp Leu Ser Ala Asp Ala Pro Val Phe Gln Gly Leu Ser Leu Val
                   -20
                                       -15
Ser His Ala Pro Gly Glu Ala Leu Ala Arg Ala Pro Arg Thr Ser Cys
Ser Gly Ser Gly Glu Arg Glu Ser Pro Glu Arg Lys Leu Leu Gln Gly
                           15
Pro Met Asp Ile Ser Glu Lys Leu Phe Cys Ser Thr Cys Asp Gln Thr
                       30
Phe Gln
40
<210> 1198
<211> 56
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -35..-1
<400> 1198
Met Leu Leu His Tyr Leu Lys Leu Lys Gly Asp Gln Trp Lys Leu Ser
                   -30
                                        -25
Ser Val Ser Thr Leu Ile Leu Phe Ile Phe Ile Gly Ser Leu Gln Pro
              -15
                                   -10
Val Pro Thr Arg Phe Lys Arg Phe Ser Cys Leu Xaa His Leu Ser Ser
Arg Asp His Arg Gln Ala Leu Arg
   15
                       20
<210> 1199
<211> 184
<212> PRT
<213> Homo sapiens
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<221> SIGNAL
<222> -153..-1
<400> 1199
Met Ala Glu Gly Asp Asn Arg Ser Thr Asn Leu Leu Ala Ala Glu Thr
                               -145
Ala Ser Leu Glu Glu Gln Leu Gln Gly Trp Gly Glu Val Met Leu Met
       -135
                           -130
                                               -125
Ala Asp Lys Val Leu Arg Trp Glu Arg Ala Trp Phe Pro Pro Ala Ile
   -120
                       -115
                                           -110
Met Gly Val Val Ser Leu Val Phe Leu Ile Ile Tyr Tyr Leu Asp Pro
                   -100
                                       - 95
Ser Val Leu Ser Gly Val Ser Cys Phe Val Met Phe Leu Cys Leu Ala
               -85
                                   -80
Asp Tyr Leu Val Pro Ile Leu Ala Pro Arg Ile Phe Gly Ser Asn Lys
           -70
                               -65
Trp Thr Thr Glu Gln Gln Arg Phe His Glu Ile Cys Ser Asn Leu
                           -50
Val Lys Thr Arg Arg Arg Ala Val Gly Trp Trp Lys Arg Leu Phe Thr
                       -35
                                           -30
Leu Lys Glu Glu Lys Pro Lys Met Tyr Phe Met Thr Met Ile Val Ser
                   -20
                                       -15
Leu Ala Ala Val Ala Trp Val Gly Gln Gln Val His Asn Leu Leu Leu
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1
Thr Tyr Leu Ile Val Thr Ser Leu Leu Leu Pro Gly Leu Asn Gln
        10
                             15
                                                 20
 His Gly Ile Ile Leu Lys Tyr Ile
 <210> 1200
 <211> 101
 <212> PRT
 <213> Homo sapiens
 <220>
 <221> SIGNAL
 <222> -26..-1
 <400> 1200
 Met Ala Ala Leu Lys Ala Leu Val Ser Gly Cys Gly Arg Leu Leu Arg
                         -20
                                             -15
 Gly Leu Leu Ala Gly Pro Ala Ala Thr Ser Trp Ser Arg Leu Pro Ala
                -5
 Arg Gly Phe Arg Glu Val Val Glu Thr Gln Glu Gly Lys Thr Thr Ile
            10
 Ile Glu Gly Arg Ile Thr Ala Thr Pro Lys Glu Ser Pro Asn Pro Pro
                             30
 Asn Pro Ser Gly Gln Cys Pro Ile Cys Arg Trp Asn Leu Lys His Lys
 Tyr Asn Tyr Asp Asp Val Leu Leu Ser Gln Phe Ile Arg Pro His
                    60
 Gly Gly Met Leu Pro
 <210> 1201
 <211> 44
 <212> PRT
 <213> Homo sapiens
<220>
 <221> SIGNAL
 <222> -23..-1
 <400> 1201
Met Gly Ser Leu Leu Phe Ile Arg Gln Thr Leu Val Gly Phe Lys Gln
            -20
                                -15
Val Val Ala Trp Thr Phe Ala Ser Asp Ser His Cys Xaa Xaa Val Xaa
        -5
Met Val Xaa Xaa Ser Gln Leu Xaa Asn Pro Pro Leu
 <210> 1202
 <211> 48
 <212> PRT
 <213> Homo sapiens
 <220>
 <221> SIGNAL
 <222> -24..-1
 <400> 1202
Met Leu Ala Arg Ala Ala Glu Xaa Thr Gly Ala Leu Leu Leu Arg Gly
                -20
                                    -15
Ser Leu Leu Ala Ser Xaa Arg Ala Xaa Xaa Pro Pro Leu Gly Leu
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Xaa Arg Asn Thr Xaa Gly Thr Val Arg Ala Ala Ala Gly Gly Leu Gly

552

10 15 20

<210> 1203 <211> 28

<212> PRT

<213> Homo sapiens

<220>

<221> SIGNAL

<222> -17..-1

<400> 1203

Met Asn Ala Ser Leu Leu Ser Phe Cys Leu Cys Ser Asp Phe Ile Ser
-15 -10 -5

Gln Asp Ala Leu Leu Thr Val Ile Phe Pro Pro 1 5 10

<210> 1204

<211> 79

<212> PRT

<213> Homo sapiens

<220>

<221> SIGNAL

<222> -60..-1

<400> 1204

Met Leu Asn Met Glu Pro Tyr Thr Val Ser Gly Met Ala Arg Gln Asp
-60 -55 -50 -45

Ser Ser Ser Glu Val Gly Glu Asn Gly Arg Ser Val Asp Gln Gly Gly
-40 -35 -30

Gly Gly Ser Pro Arg Lys Lys Val Ala Leu Thr Glu Asn Tyr Glu Leu
-25 -20 -15

Val Gly Val Ile Val His Ser Gly Gln Ala His Ala Gly His Tyr Tyr
-10 -5 1

Ser Phe Ile Lys Asp Arg Arg Gly Cys Gly Lys Gly Lys Trp Leu 10 15

<210> 1205

<211> 23

<212> PRT

<213> Homo sapiens

<220>

<221> SIGNAL

<222> -20..-1

<400> 1205

Met Xaa Xaa Ala His Phe Ser Leu His Leu Xaa Ser Ser Arg Xaa Pro
-20 -15 -10 -5

Pro Ile Leu Ala Ser Pro Val

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<210> 1206

<211> 33

<212> PRT

<213> Homo sapiens

<220>

<221> SIGNAL

<222> -17..-1

<400> 1206

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Met Ile Arg Pro Val Cys Glu Leu Ser Ile Phe Phe Thr Tyr Val Leu
   -15
                 -10
Ala Ile Tyr Ile Ser Pro Ser Val Asn Cys Leu Phe Ile Ser Phe Pro
                  5
Ala
<210> 1207
<211> 84
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -29..-1
<400> 1207
Met Arg Gly Cys Gln Leu Leu Gly Leu Arg Ser Ser Trp Pro Gly Asp
              -25
                                   -20
Leu Leu Ser Ala Arg Leu Leu Ser Gln Glu Lys Arg Ala Ala Glu Thr
           -10
His Phe Gly Phe Glu Thr Val Ser Glu Glu Glu Lys Arg Gly Asp Leu
                      10
Thr Ser Val Val Ser Leu Glu Tyr Pro Glu Val Gln Leu Gln Gly Gln
                   25
Arg Val Tyr Ala Phe Leu Ser Pro Ile Cys Thr Tyr Gly Ser Glu Gly
               40
                                   45
Cys Ser Leu Lys
<210> 1208
<211> 55
<212> PRT
<213> Homo sapiens
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<221> SIGNAL
<222> -35..-1
<400> 1208
Met Glu Asn Leu Pro Phe Pro Leu Lys Leu Leu Ser Ala Ser Ser Leu
                   -30
                                    -25
Asn Thr Pro Ser Ser Thr Pro Trp Val Leu Asp Ile Phe Leu Thr Leu
                                  -10
               -15
Val Phe Ala Leu Gly Phe Phe Phe Leu Leu Pro Tyr Phe Ser Tyr
          1
Leu Arg Cys Asp Asn Pro Pro
  15
                       20
<210> 1209
<211> 20
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -13..-1
<400> 1209
Met Cys Val Cys Val Phe Ala Ile Phe Gly Val Arg Cys Cys Val Cys
          -10
Val Arg Cys Ile
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WO 99/53051 554 <210> 1210 <211> 46 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -44..-1 <400> 1210 Met Ile Cys Ile Phe Tyr Ser Lys Ile Ser Ile Ser Val Gly Cys Gly -35 -30 Arg Thr Ala Ala Glu Gln Val Gly Cys Lys Gln Arg Ser Phe His Xaa -20 Pro Cys Pro Leu Leu Phe Pro Gly Ala Cys Phe Pro Cys Pro <210> 1211 <211> 29 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -16..-1 <400> 1211 Met Asn Leu Ile Cys Val Ser Leu Met Ala Ser Asp Gly Ala Ser Ser -10 Pro Val Leu Gly Gly Ser Ser His Ser Ser Ser Xaa Xaa <210> 1212 <211> 59 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -47..-1 <400> 1212 Met Gly Ser Val Thr Gly Ala Val Leu Lys Thr Leu Leu Leu Ser -45 -40 Thr Gln Asn Trp Asn Arg Val Glu Ala Gly Asn Ser Tyr Asp Cys Asp -25 -20 Asp Pro Leu Val Ser Ala Leu Pro Gln Ala Ser Phe Ser Ser Ser Ser -15 -10 Glu Leu Ser Ser Ser His Ser Pro Gly Phe Ala <210> 1213 <211> 47 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -31..-1

<400> 1213 Met Met Ser Glu Xaa Ser Gln Asp Leu Val Val Lys Cys Ala Pro Pro -30 -25

555. Xaa Pro Phe Phe Leu Phe Leu Phe Ser Ser Cys Asp Val Pro Val -10 -5 Pro Leu His Leu Leu Gln Trp Leu Gln Ser Phe Leu Arg Pro Arg 10 <210> 1214 <211> 59 <212> PRT <213> Homo sapiens

<220>

<221> SIGNAL

<222> -27..-1

<400> 1214

Met Phe Arg Cys Val Arg Phe Leu Pro Ser Gly Gly Phe Val Val Leu -20 -15

Leu Thr Ser Gly Val Lys Pro Gln Thr Phe Ala Val Ser Val Thr Ala -5 1

Leu Lys Gly Gly Met Pro Gly Val Val His Ser Ser Gly Gly Phe Val 10 15

Val Leu Leu Thr Ser Gly Ala Xaa Cys Arg Pro 30

<210> 1215

<211> 52

<212> PRT

<213> Homo sapiens

<220>

<221> SIGNAL

<222> -30..-1

<400> 1215

Met Arg Val Gly Arg Arg Glu Gly His Pro Leu Phe Pro Asn Val Pro -25 -20

Arg Cys Leu Phe Leu Asn Ala Arg Leu Ala Gly Thr Leu Cys Gln Leu -10 -5

Lys Leu Leu Gln Phe Gly Arg Leu Gly Asn Thr Glu Ser His Leu His 10 15

Gly Leu Ala Gly

20

<210> 1216

<211> 33

<212> PRT

<213> Homo sapiens

<220>

<221> SIGNAL

<222> -31..-1

<400> 1216

Met Tyr Phe Asp Ile Gln Ile Val Ser Asp Val Val Ser Gly Ile Pro -20 -25

Phe Lys Leu Cys Pro Leu Thr Cys Pro His His Ser Leu Ser Thr -15 -10 -5

Val

<210> 1217

<211> 47

<212> PRT

<213> Homo sapiens

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<220>
<221> SIGNAL
<222> -31..-1
<400> 1217
Met Leu Phe Ile Phe Ser Asp Ile Asp Trp Lys Met Asp Leu Cys Phe
                     -25
Phe Ser Phe Ser Pro Phe Leu Pro Ser Leu Pro Leu Leu Glu Ala Glu
                    -10
                                        - 5
Arg Met Arg Val Ser Asp Gln Leu Gln Tyr Thr Thr Gly Xaa Gly
                                10
<210> 1218
<211> 61
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -36..-1
<400> 1218
Met Glu Leu Glu Ala Met Ser Arg Tyr Thr Ser Pro Val Asn Pro Ala
                        -30
Val Phe Pro His Leu Thr Val Val Leu Leu Ala Ile Gly Met Phe Phe
                    -15
                                        -10
Thr Ala Trp Phe Phe Val Tyr Glu Val Thr Ser Thr Lys Tyr Thr Arg
                                5
Asp Ile Tyr Lys Glu Leu Leu Ile Ser Leu Val Ala Arq
       15
                            20
<210> 1219
<211> '38
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -17..-1
<400> 1219
Met Lys Gly Ala Leu Lys Leu Ile Ser Thr Asn Phe Ser Leu Cys Gln
       -15
                            -10
Ser Val Gln Cys Pro Ser Glu Glu Thr Ile Thr Asp Leu Val Ser Val
   1
                                        10
Pro Cys Gln Xaa Gly Leu
                20
<210> 1220
<211> 93
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -69..-1
<400> 1220
Met Thr Ser Gln Pro Val Pro Asn Glu Thr Ile Ile Val Leu Pro Ser
                -65
                                 . -60
Asn Val Ile Asn Phe Ser Gln Ala Glu Lys Pro Glu Pro Thr Asn Gln
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557
Gly Gln Asp Ser Leu Lys Lys His Leu His Ala Glu Ile Lys Val Ile
       -35
                       -30
                                                -25
Gly Thr Ile Gln Ile Leu Cys Gly Met Met Val Leu Ser Leu Gly Ile
                       -15
                                            -10
Ile Leu Ala Ser Ala Ser Phe Ser Pro Asn Phe Thr Gln Val Thr Ser
                    1
Thr Leu Leu Asn Ser Ala Tyr Pro Phe Ile Gly Pro Gly
            15
                                20
<210> 1221
<211> 55
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -40..-1
<400> 1221
Met Val Asp Glu Cys Leu Thr Glu Pro Val Trp Gly Ser Lys Arg Gln
                                        -30
                    -35
-40
Gly. Cys Ser Ser Gln Ala Glu Ala Ser Cys Asp Ile Val Ser Ala Ala
                                    -15
                -20
Cys Lys Cys Gly Ser Ser Gln Ala Ala Ile Asp Cys Glu Thr Ser Ser
            -5
Cys Ser Glu Asp Phe Pro Val
    10
<210> 1222
<211> 31
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -14..-1
<400> 1222
Met Ala Trp Trp Phe Ser Gly Thr Phe Pro Leu Thr His Pro Cys Ser
                                    -5
                -10
Gly Tyr Gly Ser Leu Met Ala Pro Ser Ser Pro Thr Pro Ser Gly
    . 5
                            10
                                                15
<210> 1223
<211> 78
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -57..-1
<400> 1223
Met Val Ala Lys Asp Tyr Pro Phe Tyr Leu Thr Val Lys Arg Ala Asn
                                                -45
                            -50
Cys Ser Leu Glu Leu Pro Pro Ala Ser Gly Pro Ala Lys Asp Ala Glu
                        -35
                                            -30
Glu Pro Ser Asn Lys Arg Val Lys Pro Leu Ser Arg Val Thr Ser Leu
                    -20
                                        -15
Ala Asn Leu Ile Pro Pro Val Lys Ala Thr Pro Leu Lys Arg Phe Ser
                -5
                                    1
Gln Thr Leu Gln Arg Ser Ile Ser Phe Arg Ser Glu Ser Ala
                            15
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<210> 1227

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<210> 1224
<211> 94
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -28.:-1
<400> 1224
Met Ser Pro Ala Phe Arg Ala Met Asp Val Glu Pro Arg Ala Lys Gly
                                -20
            -25
Val Leu Leu Glu Pro Phe Val His Gln Val Gly Gly His Ser Cys Val
        -10
                            -5
Leu Arg Phe Asn Glu Thr Thr Leu Cys Lys Pro Leu Val Pro Arg Glu
                                         15
His Gln Phe Tyr Glu Thr Leu Pro Ala Glu Met Arg Lys Phe Thr Pro
                                    30
                25
Gln Tyr Lys Gly Gln Ser Gln Arg Pro Leu Val Ser Trp Pro Ser Leu
Pro His Phe Phe Pro Trp Ser Phe Pro Leu Trp Pro Gln Gly
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 Met Leu Gly Gly Ala Val Ile Ala Gly Arg Pro Leu Gly Arg Trp Glu
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 Ser Thr Ala Gln Xaa Ile Leu Ala Phe Leu Gln Ser Pro Arg Ala Ile
                                 -10
             -15
 Leu Pro Gly Asn Phe Phe Glu Lys Asn Ala Gln Ile Gln Gly Gly Pro
                                            10
 Trp Gly Gly Gly Ser Gly Lys Thr Cys Ala Pro Gly Arg Xaa Asp Pro
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                                         25
 Gly Trp Glu Cys Gly Ala Gly Gly Gly Xaa Gly Glu Ala Ala Gly Ser
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 Arg Xaa Arg Xaa Ser
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 <400> 1226
 Met Ser Met Ala Cys Phe Phe His Leu Phe Val Ser Ser Leu Ile Ser
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 Phe Glu Gln Cys Phe Xaa Met Leu Arg Lys Leu Leu Lys Ile Ile
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<211> 79
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 <213> Homo sapiens
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 Met Gly Ser Arg Gly Asp Pro Leu Ile Cys Gly Leu Gln Arg Ser Val
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 -45
 Gly Glu Val Trp Phe Pro Gly Trp Gly His Thr Ile Thr His Cys Phe
                 -25
                                     -20
 Pro Trp Leu Glu Val Gly Leu Phe Phe Trp Leu His Ala Ala Pro Gly
             -10
                                .-5
 Arg Ala Ile Ala Leu Pro His Phe Ser Ser Phe Ser Val Gly Gln Xaa
                                             15
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 Val His Leu Val Ser Pro Leu Xaa Xaa Leu Asp Ile Ser Val Glu
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 <222> -19..-1
 <400> 1228
 Met His Leu Leu Gln Glu Glu Leu Leu Leu Leu Pro Arg Gly Leu
                 -15
                                     -10
 Cys Gln Val Cys Pro Arg Leu Cys Leu Gln Arg Xaa Val Gly Glu Leu
            ` 1
                                                 10
 Gln Xaa Xaa Xaa Pro Asp Val Gly Thr Ala Leu Leu Pro Asp Val Asn
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 Arg Thr Ser Cys Thr Thr Trp
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 Met Cys Leu Ser Cys Ile Gln Gly Ser Phe Phe Val Glu Ile Leu Gln
             -25
                                 -20
                                                      -15
 Leu Val Thr Arg Leu Leu Ser Pro Ser Gln Ser Thr Gln Thr His
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 Thr His Thr His Thr His Thr
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 <211> 39
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<400> 1233

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Met Thr Ile Leu Arg Glu Met Xaa Xaa Ser Leu Tyr Val Leu Glu Ala
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Lys Asp Thr Ala Ile Leu Leu Leu Val Xaa Val Ser Asp Lys Asn Glu
                                            -5
                        -10
Gln Gln Leu Gly Arg Gly Val
<210> 1231
<211> 51
<212> PRT
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<221> SIGNAL
<222> -29..-1
<400> 1231
Met Arg Leu Ser Ser Cys Gly Leu Pro Val Lys Thr Leu Pro Phe
                                    -20
Ile Cys Cys Asn Leu Tyr Phe Leu Leu Phe Cys Arg Ser Ser Phe Leu
                                 - 5
            -10
Tyr Phe Gly Tyr Asp Pro Ile Asn Thr Tyr Met Tyr Tyr Asn Val Phe
                        10
   5
 Ser His Ser
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 <210> 1232
 <211> 89
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 <222> -68..-1
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 Met Leu Leu Thr Arg Pro Ala Val Ser Ala Gly Gly Ala Xaa Arg Phe
                                 -60
             -65
 Ser Pro Gly Ser Arg Gly Arg Gly Ser Asp Leu Glu Arg Gly Leu Cys
                             -45
         -50
 Pro Ala His Pro Gly Ala Pro Pro Leu Pro Arg Pro Pro Asp Arg Leu
                                              -25
                         -30
 Pro His Ser Phe Ser Pro Thr Gly Cys Leu Leu Xaa Pro Leu Leu Val
                                          -10
                     -15
 Ser Cys Leu Gly Ser Leu Leu Pro Val Thr Gln Thr Leu Gly Ser Phe
                                 5
  Ser Ala Gly Pro Cys Phe Arg Thr Leu
  <210> 1233
  <211> 46
  <212> PRT
  <213> Homo sapiens
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  <221> SIGNAL
  <222> -25..-1
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Met His Ser Leu Cys Pro Leu Ser Gln Phe Leu Pro Ile Leu Xaa Ser

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-20
                                       -15
Leu Ser Ser Ser Val Pro Ser Arg Ala Gly Ser Ala Phe Pro Ser Ala
            - 5
                                1
Leu Gly Pro Leu Tyr Gln Pro Leu Leu Gly Pro Pro Ala Trp
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Met Arg Thr Gln Val Tyr Glu Gly Leu Cys Lys Asn Tyr Phe Ser Leu
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                                  -35
Ala Val Leu Gln Arg Asp Arg Ile Lys Leu Leu Phe Phe Asp Ile Leu
                               -20
           -25
Val Phe Leu Ser Val Xaa Leu Leu Phe Leu Leu Phe Leu Val Asp Ile
  -10
                           - 5
Met Ala Asn Xaa Thr Thr Ser Leu Gly Arg Pro
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<210> 1235
<211> 109
<212> PRT
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<222> -45..-1
Met Gly Gln Phe Thr Ala Ala Met Val Gly Arg Ile Ser Cys Leu Gly
                    -40
                                        -35
Val Trp Lys Leu Pro Arg Val Glu Ser Cys Ser Gln Pro Ala Arg Pro
               -25
                                   -20
Leu Leu Ser Leu Ala Gln Thr Thr Thr Lys Thr Thr Ala Thr Thr Thr
                               -5
Thr Thr Thr Lys His Ala Thr Cys Ala Leu Ala Tyr Thr Asn Thr Pro
                        10
Thr Glu Pro Xaa Gln Ala Asp Lys Ala Ser Arg Arg Ala Ser Gly Xaa
                                       30
Leu Xaa Xaa Ala Ala Arg His Ile Pro Trp His Gly Ala Thr Ala Ala
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                                   45
Gln Leu Pro Ala Pro Pro Pro Ser Val Ile Ser Ala Leu
<210> 1236
<211> 28
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -18..-1
<400> 1236
Met Leu Ile Phe Ile Ile Ala Ile Leu Phe Pro Asn Ser Gly Ser Cys
                               -10
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Phe Ala Phe Ser Cys His Val Ser Phe Phe Phe

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<210> 1237
<211> 58
<212> PRT
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<221> SIGNAL
<222> -15..-1
<400> 1237
Met Val Arg Cys Ala Cys Phe Pro Phe Pro Phe Ala Phe Cys His
                                         -5
                    -10
-15
Asp Cys Lys Phe Leu Gly Ala Ser Gln Ser Cys Phe Leu Leu Ser Arg
                                 10
Gln Asn Cys Val Ser Thr Gly Xaa Pro Ser Ser Lys Ser Asp Ile Asn
                             25
       20
Ser Arg Ser Gly Ser Cys Ser Leu Ala Arg
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<210> 1238
<211> 98
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<213> Homo sapiens
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<400> 1238
Met Val Ser Leu Arg Val Gly Ala Ser Pro Phe Arg Phe Pro Leu Ala
                             -20
Pro Leu Xaa Leu Val Phe Ile Ser Leu Leu Pro Ala Pro Phe Phe Pro
                                             1
                         -5
Thr Leu Ser Phe Pro Cys Cys Cys Val Ser Trp Leu Phe Ser Leu Ser
                                     15
                10
Val Xaa Val Ser Leu Arg Leu Ser Leu Xaa Val Ser Cys Leu Ser Leu
                                 30
 Trp Cys Leu Leu Val Leu Phe Leu Ser Pro Thr Leu Tyr Val Ser Asp
                            45
 Ser Phe Cys Ser Phe Cys Val Leu Pro Ile Ala Leu Cys Pro Xaa Ala
                         60
 Arg Ser
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 <210> 1239
 <211> 72
 <212> PRT
 <213> Homo sapiens
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 <222> -54..-1
 <400> 1239
 Met Ala His Pro Cys Leu Ala Pro Ala Glu Pro Ser Thr Leu Ser Gln
                                      -45
 Thr Xaa His Pro Ile Gln Arg Thr Leu Thr Thr Phe Pro Gln Ala Trp
                                                      -25
                                 -30
 Val Leu Thr Ser Ser Phe Ser Ile Gln Pro Gly Leu Ala Phe Leu Ala
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-15 Ile Leu Thr Val Leu Ala Lys Pro Gly Ser Ser Xaa Trp Ser Pro Gly

563 Gln Phe Thr Pro His Ser Leu Leu 15 <210> 1240 <211> 35 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -31..-1 <400> 1240 Met His Phe Pro Ile Gln Ala Thr Phe Xaa Tyr Ser Pro Thr Asp Ser -20 -25 Leu Cys His Leu Tyr Xaa Ser Leu Phe Ser Ser Phe Leu Cys Ser Thr -10 -5 Pro Ala Arg <210> 1241 <211> 61 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -36..-1 <400> 1241 Met Ala Leu His Ile Leu Glu Cys Glu Arg Asn Val Cys Phe Val Ala -25 -30 Val Arg Gln Pro Ala His Glu Ser Cys Phe Val Pro Ser Leu Val Thr -15 -10 Gly Ala Leu Gln Gln Ser Gln Thr Gln His Pro Pro Trp Val Cys Pro 5 1 Gln Val Gln Gly Ser Tyr Pro Ser Trp Lys Asn Arg Gly 20 <210> 1242 <211> 58 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -32..-1 <400> 1242

Met Ser Cys Thr His Ser Ser Ser Asn Leu Gly Lys Phe Ser Val His -25 -20 -30 Arg Glu Tyr Arg Val Leu Xaa Leu Cys Asn Ser Arg Val Ser Phe Thr -10 -5 Arg Xaa His Val Lys Arg Pro Pro Xaa Arg Leu Cys Val Ser Ser Lys

Gly Cys Leu Phe His Leu Gly Ala Gly Arg

<210> 1243 <211> 40 <212> PRT <213> Homo sapiens 564

<220> <221> SIGNAL <222> -19..-1 <400> 1243 Met Leu Lys Lys Leu Ser Ala Phe Pro Leu Leu Val Ile Ile Leu -15 -10 Leu Phe Gln Lys Gln Xaa Gly Leu Leu Lys Asn Tyr Xaa Ser Pro Gln 5 Arg Gln Val Leu Phe Cys Asn Arg 15 <210> 1244 <211> 29 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -18..-1 <400> 1244 Met Ser Tyr Phe Arg Cys Ile Phe Leu Ala Val Leu Ser Lys Ile Ser -10 -15 Trp Ala Val Asn Met Cys Ser Leu Ile Ser Gly Ser Ser <210> 1245 <211> 39 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -34..-1 <400> 1245 Met Leu Cys Ile Met Phe Gly Ile Glu Thr Asn Glu Ile Thr Lys Met -25 -30 -20 Thr Met Ser Phe Leu Leu Phe Leu Ser Ile Ser Leu Ile Thr Leu Tyr -15 Tyr Ser Ser Glu Ala Cys Gly 1 · <210> 1246 <211> 90 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -39..-1 <400> 1246 Met Cys Gln Ala Arg Ile Ala Leu Asp Arg Cys Asn Leu Arg Thr Ala -30 -35 Phe Ile Leu Phe Xaa Leu Ile Leu Ser His Tyr Val Phe Xaa Leu Leu -20 -15 -10 Ala Pro Phe Leu Thr Arg Ser Ser Pro Ser Trp Asn Ser Tyr Gly Thr 1

Leu Ala Pro Glu Thr Thr Asn Ser Ser Leu Lys Phe Ser Asn Ser Asn

Asn Gly Ile Ser Asp Leu Ala Xaa Leu Tyr Phe Ser His Val Xaa Lys

20

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Ile Gly Ser Ala Ser Thr Met Gly Tyr Gly
<210> 1247
<211> 99
<212> PRT
<213> Homo sapiens
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<222> -24..-1
<400> 1247
Met Val Lys Ser Val Ile Phe Leu Ser Phe Trp Gln Gly Met Leu Leu
                -20
                         -15
Ala Ile Leu Glu Xaa Cys Gly Ala Ile Pro Lys Ile His Ser Ala Arg
Val Ser Val Gly Glu Gly Thr Val Ala Ala Gly Tyr Gln Asp Phe Ile
                       15
Ile Cys Val Glu Met Phe Phe Ala Ala Leu Ala Leu Arg His Ala Phe
Thr Tyr Lys Val Tyr Ala Asp Lys Arg Leu Asp Ala Gln Val Pro Thr
                                   50
Tyr Gly Pro Tyr Gly Arg Cys Ala Pro Met Lys Ser Ile Ser Ser Ser
Leu Lys Glu
        75
<210> 1248
<211> 88
<212> PRT
<213> Homo sapiens
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<221> SIGNAL
<222> -86..-1
<400> 1248
Met Asp Met Arg Trp His Cys Glu Asn Ser Gln Thr Thr Asp Asp Ile
                        -80
                                           -75
Leu Val Ala Ser Ala Glu Cys Pro Ser Asp Asp Glu Asp Ile Asp Pro
                   -65
                                       -60
Cys Glu Pro Ser Ser Gly Gly Leu Ala Asn Pro Thr Arg Ala Gly Gly
               -50
                                   -45
Arg Glu Pro Tyr Pro Gly Ser Ala Glu Val Ile Arg Glu Ser Ser Ser
                               -30
           -35
Thr Thr Gly Met Val Val Gly Ile Val Ala Ala Ala Ala Leu Cys Ile
       -20
                                               -10
Leu Ile Leu Leu Xaa Ala Met Tyr
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<210> 1249
<211> 125
<212> PRT
<213> Homo sapiens
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<221> SIGNAL
<222> -20..-1
Met Ala Trp Thr Pro Leu Trp Pro Thr Leu Leu Thr Leu Cys Ile Gly
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 Ser Val Val Ser Ser Asp Leu Thr Gln Asp Pro Ala Val Ser Val Ala
 Leu Gly Gln Arg Val Arg Ile Thr Cys Gln Gly Asp Asn Leu Glu Glu
 Tyr Phe Ala Ser Trp Tyr Arg Gln Arg Pro Gly Gln Ala Pro Val Leu
 Val Ile Tyr Gly Lys Asn Asn Arg Pro Ser Gly Ile Pro Xaa Arg Xaa
                     50
                                         55
 Ser Gly Ser Lys Ser Gly Asn Thr Ala Leu Leu Thr Ile Xaa Gly Ala
                 65
                                     70
 Gln Ala Glu Asp Xaa Ala Asp Tyr Tyr Cys Ser Xaa Arg Asp His Thr
                                 85
 Asp Asn Arg Trp Val Phe Gly Gly Gly Thr Arg Leu Thr
                             100
 <210> 1250
 <211> 70
 <212> PRT
 <213> Homo sapiens
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 <222> -20..-1
 <400> 1250
 Met Glu Ala Glu Phe Tyr Met Xaa Ile Leu Thr Cys Leu Ile Phe Arg
                     -15
                                         -10
 Asn Ser Glu Gly Phe Gln Ile Xaa His Val Gln Lys Gln Gln Cys Leu
 Phe Lys Asn Glu Lys Val Val Gly Ser Cys Asn Arg Thr Ile Gln
                             20
 Asn Gln Gln Trp Met Trp Thr Glu Asp Glu Lys Leu Leu His Val Lys
                         35
 Ser Ala Leu Cys Leu Ala
 <210> 1251
 <211> 19
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -17..-1
<400> 1251
Met Cys Val Cys Ala Cys Ala Leu Cys Val Trp Leu Cys Val Lys Ser
   _ -15
Cys Ser Ile
    1
<210> 1252
<211> 34 ·
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -21..-1
<400> 1252
Met Ile Ser Asp Val Gln His Leu Phe Ile Tyr Leu Leu Ala Phe Cys
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567

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-15
Met Pro Ser Leu Glu Lys Cys Leu Tyr Gly Ser Leu Ala His Phe Phe
-5
                  1
                                 5
Phe Phe
<210> 1253
<211> 28
<212> PRT
<213> Homo sapiens
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<221> SIGNAL
<222> -15..-1
<400> 1253
Met Pro Leu Phe Arg Val Leu Phe Ser Xaa Thr Cys Ala Leu Xaa Gln
-15 -10
                                      -5
Asp Phe Arg Met Gln Pro Cys Pro Pro Thr Pro Lys
           5
<210> 1254
<211> 30
<212> PRT
<213> Homo sapiens
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<221> SIGNAL
<222> -24..-1
<400> 1254
Met Trp Tyr Val Glu Met Trp Val Ser Phe Phe Leu Leu Phe Tyr Val
              -20
                        -15 -10
Leu Leu Phe Arg Asn Leu Tyr Thr His Thr His His Thr Gly
                              1
<210> 1255
<211> 54
<212> PRT
<213> Homo sapiens
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<222> -30..-1
<400> 1255
Met Ala Ala Arg Val Gly Ala Phe Leu Lys Asn Ala Trp Asp Lys Glu
                 -25
                                     -20
Pro Val Leu Val Val Ser Phe Val Val Gly Gly Leu Gly Cys Asn Xaa
               -10
                                  ~5
Ala Pro Ile Glu Pro Leu Leu Gln Val Leu Arg His Asp Gln Gln Gly
                          10
His Ala Leu Gln Leu Xaa
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<210> 1256
<211> 103
<212> PRT
<213> Homo sapiens
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<222> -23..-1
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<211> 42

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Met Gln Ala Arg Arg Trp Glu Ser Trp Met Trp Thr Cys Val Ala Pro
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                                -15
Val Tyr Pro Ala Cys Ser Gly Arg Arg Ala Xaa Ala Val Xaa Gln Xaa
Xaa Pro Arg Leu Gly Xaa Xaa Leu Pro Gly Pro Gly Xaa Glu His Leu
                    15
Ala His Val Cys Gly Leu Pro Ala Gly Glu Ala Gly Arg Gly Arg Gly
                                    35
Val Glu Arg Pro Gln Glu Lys Arg Ala Asp Lys Ala Val Xaa Val Arg
                                50
Arg Gly Leu Gly Gly Ala Gly Leu Pro Gly Gly Asp Thr Pro Arg Gly
                            65
Pro Pro Met Ser Thr Trp Pro
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<210> 1257
<211> 16
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<213> Homo sapiens
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<222> -14..-1
<400> 1257
Met Phe Leu Phe Phe Gly Asn Ser Pro Cys Cys Gly Ala Thr Gly
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<210> 1258
<211> 40
<212> PRT
<213> Homo sapiens
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<221> SIGNAL
<222> -25..-1
<400> 1258
Met Gly Leu Ser His His Arg Val Ser Ala Pro Ser Ser Leu Ser Leu
                    -20
                                       -15
Ser Leu Ser Ala Ser Leu Ile Ile Ser Pro Ser Pro Ser Ala Ser Pro
               -5
                                    1
Ser Leu Leu Xaa Pro Pro Xaa Arg
       10
<210> 1259
<211> 32
<212> PRT
<213> Homo sapiens
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<222> -23..-1
<400> 1259
Met Phe Val Phe Leu Val Gly Thr Pro Cys Leu Ser Met Leu Leu Arq
           -20
                                -15
Leu Val Ser Asn Ser Arg Pro Pro Val Met Arg Pro Pro Arg Pro Gly
<210> 1260
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<212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> ~33..-1 <400> 1260 Met Lys Phe Thr His Phe Lys Cys Thr Ile Arg Leu Leu Leu Leu Tyr -30 -25 Leu Gln Asn Pro Val Thr Ile Thr Ile Leu Phe Leu Ile Val Ser Met -15 -10 -5 Ala Leu Lys Ile Asn His Ile Pro Lys Gly , 5 1 <210> 1261 . <211> 42 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -14..-1 <400> 1261 Met Ser Cys Met Ser Leu Phe Pro Cys Cys Pro Ala Gln Ser Lys Asn -10 -5 Tyr Met Leu Leu Phe Ile Ile Leu Leu Pro Thr Gln Phe Leu Tyr 10 Ser Lys Leu Val Thr Ile Cys Cys Phe <210> 1262 <211> 26 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -14..-1 <400> 1262 Met Leu Val Cys Cys Thr Ile Asn Ser Ser Phe Ala Leu Gly Ile Ser -10 - 5 Arg Asn Ala Ile Pro Leu Pro Ala Pro Gly 5 <210> 1263 <211> 69 <212> PRT <213> Homo sapiens <220> • <221> SIGNAL <222> -53..-1 <400> 1263 Met Gly Arg Gly Pro Gly Pro Leu Gln Glu Arg Ser Leu Phe Glu Xaa -50 -45 Lys Arg Gly Ala Pro Pro Ser Ser Asn Ile Glu Asp Phe His Gly Leu -35 -30 -25

Leu Pro Lys Val Ile Pro Ile Cys Ala Leu Tyr Val Ile Cys Gln Phe

-10

-15

-20

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Ile Leu Ile Arg Ser Gly Val Asn Ile Ser Met Glu Gln Val Thr Val
 Val Asp. Ala Ser Leu
             15
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 <211> 40
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 <213> Homo sapiens
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 <222> -13..-1
 <400> 1264
 Met Leu Tyr Cys Val Val Val His Ser Val Cys Cys Ala Val Tyr
            -10
                              ~5
 Tyr Phe Val Ile Ile His Thr Ile Glu His Ile Thr Tyr Leu Cys Ile
                        10
                                             15
 His Ser Thr Ile Leu Leu Cys Val
                     25
 <210> 1265
 <211> 37
 <212> PRT
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 <222> -26..-1
 <400> 1265
 Met Cys Trp Leu Arg Xaa Trp Gly Gln Ile Leu Leu Pro Val Phe Xaa
                        -20
                                  -15
 Ser Leu Phe Leu Ile Gln Leu Leu Ile Ser Phe Ser Glu Asn Gly Phe
 Ile His Ser Pro Met
             10
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 <212> PRT
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. <221> SIGNAL
 <222> -14..-1
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Met Cys Gly Leu Xaa Ile Leu Cys Gly Pro Trp Leu His Ala Ala Pro
                                    -5
 Pro Ser Pro Pro Arq
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 <210> 1267
 <211> 42
 <212> PRT
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 Met Phe His Gly Arg Val Met Ala Met Gly Xaa Leu Thr Lys His Leu
           -30
                         -25
                                            -20
 Asn Leu Asn Ile Ser Ile Ser Leu Leu Leu Met Leu Xaa Xaa Tyr Trp
                            -10
 Ser Cys Trp Ile Lys Ser Pro Pro Xaa Met
 <210> 1268
 <211> 132
 <212> PRT
 <213> Homo sapiens
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 <222> -128..-1
 <400> 1268
Met Leu Gly Arg Ser Ser Leu Leu Xaa Trp Lys Xaa Ser Pro Gly Ser
            -125
                                -120
                                          . -115
 Lys Lys Leu Val Val Ala Thr Glu Lys Asn Val Ile Ala Ala Leu Asn
     -110
                           -105
                                              -100
 Ser Arg Thr Gly Glu Ile Leu Trp Arg His Val Asp Lys Gly Thr Ala
                        -90
                                           -85
 Glu Gly Ala Val Asp Ala Met Leu Leu His Gly Gln Asp Val Ile Thr
                    -75
                                        -70
 Val Ser Asn Gly Gly Arg Ile Met Arg Ser Trp Glu Thr Asn Ile Gly
                -60
                                    -55
Gly Leu Asn Trp Glu Ile Thr Leu Asp Ser Gly Ser Phe Gln Ala Leu
            -45
                               -40
Gly Leu Val Gly Leu Gln Glu Ser Val Arg Tyr Ile Ala Val Leu Lys
        -30
                            -25
                                               -20
 Lys Thr Thr Leu Ala Leu His His Leu Ser Ser Gly His Ser Ser Gly
   -15
                        -10
                                            - 5
 Trp Thr Ser Pro
 <210> 1269
 <211> 72
 <212> PRT
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 <222> -57..-1
 <400> 1269
Met Ser Thr Thr Tyr Leu Asn Glu Asp Leu Lys Lys Lys Phe Ser Ala
       -55
                            -50
 Val Ile Glu Gln Val Leu Phe Ala His Leu Ser Pro Leu His Val Trp
                        -35
                                           -30
Leu Gln Leu Arg Ser Leu Cys Glu Xaa Leu Thr Cys Ile Trp Val Arg
                   ~20
                                       -15
Phe Asn Phe Leu Ala Ser Ser Gln Ala Cys Ser Lys Cys Asn Ser Ser
               -5
Phe Leu Ile Met Ser Ser Ser
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<210> 1270
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<212> PRT
<213> Homo sapiens
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      -30
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                                                -20
 Ala Lys Leu Leu Glu Leu Val Ala Thr Leu Pro Asp Asp Val Gln Pro
    -15
                        -10
                                            - 5
 Gly Pro Asp Phe Tyr Gly Xaa Xaa Trp Lys Leu Tyr Leu Ser Leu Pro
                                    10
 Ser Trp Glu Xaa Phe Val Cys His Phe Leu Met Glu Thr Val Leu Val
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Val Lys Xaa Arg Val Tyr Xaa Val
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 Met Ala Ala Tyr Phe Ala Val Trp Ala Ser Val Ala Ser Pro Ala Ser
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 Ile Cys Cys Gly Xaa Trp Leu Thr Gly Leu Val Arg His Glu Arg Ile
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 Glu Ala Pro Trp Ala Arg Gly
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Met Lys Thr Gln Phe Leu Ser Trp Gly Lys Phe Ser Phe Cys Phe Gly
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Ile Leu Leu Gln Leu Leu Lys Xaa Ser Leu Lys Lys Cys Arg
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His Gly
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 Phe Cys Ile Phe Trp Xaa Glu Thr
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 Ser Arg Gly Arg Val Arg Lys Leu Gly Gly Ala Val
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Gln Val Ser Arg Leu Xaa Ala Leu Leu Ser Pro Tyr Ala Phe Thr Leu
Xaa Arg Leu Ala Ser Gly
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Met Arg Arg Phe Leu Leu Tyr Ala Thr Gln Gln Gly Gln Ala Lys
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Ala Ile Ala Glu Glu Met Cys Xaa Gln Ala Val Val His Gly Phe Ser
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Ala Asp Leu His Cys Ile Ser Glu Ser Asp Lys Val Ser Val Ile Gln
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Asn Thr Pro Thr Phe Ala Thr Gly Gly Arg
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 Ala Pro Thr Arg Cys Pro Arg Pro Ser
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Leu Ser Ile Pro Asp Cys Leu Pro Ala Phe Leu Trp Pro Leu Gly Ile
        1
Pro Trp Pro Asp Gly Glu Gly Leu Arg Pro Ser Arg Leu Leu Arg Thr
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Arg Glu Asn Ile Thr Pro Leu Ser Leu Phe Ala Met Leu Ser Gly Arg
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Glu Gly Ala Pro Leu Leu Val Pro Leu
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Pro Lys Gln Gly
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Met Ser Leu Gly Leu His Ser Asn Ser Trp Val Leu Asp Pro Ala Leu -20 -15

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Gly Gly Thr Arg Xaa Thr Leu Xaa Ala Leu His Ser Ala Arg Thr 15 20

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Ala Ile Leu Ala Glu Leu Thr Lys Arg Lys Glu Asn Tyr Leu Cys Arg -40 -35 -30

Thr Ser Leu Gln Gln Ile Ile Leu Glu Leu Gly Ile Asp Thr Ile Met -20

Trp Val Xaa Cys Xaa Phe Cys Phe Val Leu Phe Cys Phe Glu Thr Glu -10 -5

Ser Arg Pro Val

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Lys Trp Asp Gln Pro Ala Pro Ala Pro Leu Phe Leu Pro Pro Ala -15

-10 Ala Pro Gly Gly Glu Val Thr Ser Ser Gly Gly Ser Pro Gly Xaa Thr

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579
              1
                                                   10
 Thr Ala Ala Pro Ser Gly Ala Leu Asp Ala Ala Ala Ala Val Ala Ala
                        20
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 Lys Ile Asn Ala Met Leu Met Ala Lys Gly Lys Leu Lys Pro Thr Gln
                      35
 Xaa Ala Ser Glu Lys Leu Gln Ala Pro Gly Lys Gly Leu Thr Ser Asn
                 50
                                      55
                                                          60
 Lys Ser Lys Asp Asp Leu Val Val Ala Glu Val Glu Ile Asn Asp Val
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 Pro Leu Thr Cys Arg Asn Leu Leu Thr Arg Gly Gln Xaa Gln Asp Glu
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 Ile Ser Arg Leu Ser Gly Ala Ala Val Ser
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 Gly Ser Cys Trp Gly Gly Val Arg Cys Leu Val Arg Gly Gly Pro Asn
 Ile Gly Pro Ala Ala Gln Leu Leu Gly Gly Ile Pro Leu Cys Trp Pro
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 Pro Ala Val Thr Ala Gly Glu Val Lys Leu
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Xaa Ala Gln
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Leu Leu Ser Thr His Thr Trp Thr Asp Thr Ala Leu Ala Phe Ser Thr
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His Thr His
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 Phe Ile Ser Pro Ser Ile Gln
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Phe Val His Gly Leu Asn Ile Thr Gln Leu Val Leu Ser Gln Leu Asp
        -35
                            .-30
                                                 -25
Tyr Phe Phe His Ser Asn Leu Thr Asn Leu Val Leu Tyr Phe Leu Val
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                                             -10
His Leu Leu Phe Ser Leu Ser Leu Phe Met Pro Leu Thr
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-50

Xaa Lys Val Pro Leu Ile Gly Phe Leu Lys Arg Ile Xaa Xaa Tyr Xaa

~55

-60

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Leu Thr Val Leu Lys Pro Xaa Ser Leu Xaa Ser Xaa Ser Ala Gly Leu
 . -45
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 Val Pro Ser Glu Asp Ser Lys Lys Glu Ser Val Ser Cys Leu Ser Pro
                                -20
                    -25
 Arg Phe Trp Trp Leu Gly Ser Leu Xaa Val Thr Trp Leu Ile His
                -10
                                    -5
 Ala Ser Leu Gln Ser Leu Ser Pro Phe Ser His Ala Ile Phe Ser Cys
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 Val Ser Val Phe Ser Phe Ala Tyr Lys Asp Thr Ser His Ile Glu Leu
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 Gly Pro Ala Leu Ile Thr Ser Ser Gln Leu Pro Leu Gln Gly Thr Asn
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 Arg Met Gly Asn Leu Lys Leu Leu Phe Leu Ile Leu Ile Ala
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                            -10
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 Gly Tyr Arg
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Leu Met Leu Pro Leu Gly Cys Ala Val Arg Thr Arg Met Leu
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Trp Ile Leu Thr Thr Leu Glu Ser Leu Ala Gly Ser Val Xaa Ser Glu
                   -10
                                      -5
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                                          -15
   Tyr Phe Lys Phe Trp Gly Thr Cys Ala Glu Arg Ala Gly Leu Leu His
                  -5
   Arg Tyr Thr Arg Ala Met Glu Val Cys Cys Thr His Gln Pro Ser Ser
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   Thr Leu Gly Ile Ser Pro Asn Ala Leu Leu Pro Leu
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  Ile His Pro Xaa Xaa Cys Ala Cys Ile Cys Pro Ser Ile Gln
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  Xaa Thr Arg Thr Thr Gly Lys Xaa Val Cys Val Cys Val Cys
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  Val Cys Val Cys Val Cys
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-10

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Ser Trp Gly Cys Ser Arg Leu Arg Phe Gly Pro Pro Ala Tyr Arg Arg
  Phe Ser Ser Gly Gly Ala Tyr Pro Asn Ile Pro Leu Ser Ser Pro Leu
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  Pro Gly Val Pro Lys Pro Val Phe Ala Thr Val Asp Gly Gln Glu Lys
                      40
                                           45
  Phe Glu Thr Lys Val Thr Thr Leu Asp Asn Gly Leu Arg Val Ala Ser'
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  Gly Ser Arg Tyr
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Gly Pro Arg Tyr
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Ser Leu Leu Thr Phe Cys Leu Ile Asp Leu Ser Asn Val Asp Ser Gly
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Gly Arg Arg Ala Arg Lys Leu Leu Pro Ala Pro Arg Ala Ala Pro Arg
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                                                 -25
Thr Ala Pro Asp Tyr Pro Gly Pro Leu Arg Leu Thr Trp Leu Val Ala
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                                            -10
Ala Gly Leu Glu Gly Arg Val His Leu Ala Asp Thr Ser Ser Gly Arg
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Lys Thr Trp Pro Gly Cys Gly His Gln Trp Lys Trp Lys Ala Leu Leu
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Ile Leu Val Arg Ala Phe Pro Ala
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Arg Thr Val Cys Ser Ser Leu Arg Ser Xaa Arg Pro Cys Trp Cys Asp
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Gly Leu Arg Leu Arg
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                             -15
 Pro Ser Val Ala Gln Ser Gly Val Gln Trp Cys Asp Leu Gly Leu Leu
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                        1
 Gln Pro Pro Pro Gly Phe Lys Arg Phe Ser Cys Leu Ser Leu Leu
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 Gly Xaa Xaa Asp Cys Arg Arg Ala Pro Pro Gly
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Met Phe Leu Ser Gly Met Val Ala Gln Ile Asp Ala Asn Trp Asn Phe
           ~ 5
Leu Asp Phe Ala Tyr His Phe Thr Val Phe Val Phe Tyr Phe Gly Ala
                        15
Phe Leu Leu Glu Ala Ala Ala Thr Ser Leu His Asp Leu His Cys Asn
                                       . 35
                   30
Thr Thr Ile Thr Xaa Gln Pro Leu Leu Ser Asp Asn Gln Tyr Asn Ile
                                    50
Asn Val Ala Ala Ser Ile Phe Ala Phe Met Thr Thr Ala Cys Tyr Gly
Cys Ser Leu Gly Leu Ala Leu
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Leu Leu Val Gly Leu Phe Pro Leu Lys Cys His Xaa Ser Xaa Phe Ser
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Lys Xaa Gln Ile Ser Ser Phe Val Glu

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 Cys Ser His Ser Ile Leu Arg Pro Ser Gly Pro Gly Ala Ala Ser Leu
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 Leu Xaa Xaa Ser Asn Pro Ala Ala
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Phe Ser Asn Arg Ile Lys Ser Xaa Leu Arg Pro Pro Ala Gly
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  Leu Pro Arg Glu Cys Trp Lys Val Lys Asp Ser Lys Lys Tyr Lys Ser
              -50
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  Cys Arg Glu Ser Val Leu Pro Ala Gln Ala Cys Thr Gly Glu Ser Pro
        -35
                              -30
  Val Leu Ser Gly Val Arg Val Leu Gly Ile Arg Leu Ser Cys Val Leu
                          -15
  Ser His Leu Gln Ala Trp Asp Ser Trp Asp Asn Gln Lys Val Cys Tyr
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  Leu Gly Ala Pro Cys Phe Gly Lys Arg Leu Ser Pro Thr Thr Trp Leu
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Cys Glu Pro Arg Gly Asn Asn Pro Gln Ile Pro Leu Leu Ala Ile His
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Thr Arg Lys Lys Asn Gln His Phe Ile Thr
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Ser Val Ser Leu Xaa Xaa Xaa Xaa Xaa Gly Ser Val Arg Ile Xaa
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                      -10
                                           -5
  His Asp Ser Pro Met Xaa Ile Gly Gln Phe Pro Xaa Asn Pro Pro Ser
                                   10
  Glu His Pro Gly Ala Ser Pro Arg Arg Xaa Xaa Thr Gly Trp Xaa Pro
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  Gln Ser Trp Asp Arg Arg Val Ser Pro Ala Glu Ala Glu Thr Arg Arg
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   -40
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                      -20
  Leu Gly Phe Leu Cys Ser Leu Cys Pro His Pro His Gly
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Ser Thr Val Leu Leu Ser Gly Ser Pro Arg Ala Val Val Ser Ala Val
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Leu Lys Gln Cys Glu 75

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 Arg Ser Leu Gly Glu Cys Pro Arg Lys Arg Trp Gly Gly
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                                     -75
 Ser Val Glu Asp Gly Phe Gln Thr Val Pro Leu Ile Thr Pro Leu Glu
             -65
                                 -60
 Val Asn His Leu Gln Leu Pro Ala Pro Glu Lys Val Ile Val Lys Thr
                             -45
                                                 -40
Arg Thr Glu Tyr Gln Pro Glu Gln Lys Asn Lys Gly Lys Phe Arg Val
                        -30
                                             -25
Pro Lys Ile Ala Glu Phe Thr Val Thr Ile Leu Val Ser Leu Ala Leu
                    -15
                                         ~10
Ala Phe Leu Ala Cys Ile Val Phe Leu Val Val Tyr Lys Ala Phe Thr
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Tyr Asp His Ser Cys Pro Glu Asp Ser Ser Xaa Ser Thr Gly
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Cys Ile Tyr Trp Gly Gln Tyr Ala Thr Asp Gly Ile Gly Asn Glu Ser
-5
Val Lys Ile Leu Ala Lys Leu Leu Phe Ser Ser Phe Leu Ile Phe
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Leu Leu Met
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                                             -15
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  -10
                     -5
  Phe Phe Phe
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                                -20
 Val Phe Met Ser Lys Leu Leu Phe Ser Phe Ser Phe Leu Xaa Lys
    -10
                            - 5
 Ala Arg Met Xaa Thr Ala Ala Pro Gly
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Met Val Thr Pro Val His Ile Leu Thr Ala Val Leu Pro Leu Val Ser
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          -15
                                                  - 5
His Gln Gln Asn His Leu Gly Gly Arg Phe Ala Ser Leu Gly Ser Ser
       1
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Gly Ile Arg His Gly
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Asn Ser Phe
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  Arg Ser Ile Ile Trp Lys Ser Gly Arg Gln Gly
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                    -10
                                         -5
 His Pro Leu Gly
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                                    - 5
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                               -45
Ala Gly Asn Leu Arg Ser Leu Arg Glu Trp Pro Asp Leu Cys Cys Leu
                            -30
                                                -25
Arg Leu Phe Val Pro Asp His Thr Val Leu Ala Leu Val Cys His Ser
                        -15
Ala Ser Ile Ser Val Phe Pro Ser Gln Val Thr Cys Arg Leu Pro Arg
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Thr Gly Ser His Pro Ile Cys Val Ile Ser Gln Gly Ala Phe His Asp
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Pro His Pro Asn

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Val Val Leu Phe Ala Ser Pro Xaa Val Arg Pro Ala Ser Ser Met Ser
-10 -5 1 5

Ser Arg Leu Leu Pro Xaa Leu His Tyr Ser Asp Trp Thr Cys Trp 10 15 20

Leu Pro Glu Arg Arg 25

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<212> PRT

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Met Thr Ser Leu Leu Thr Thr Pro Ser Pro Arg Glu Glu Leu Met Thr
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-45
-40

Thr Pro Ile Leu Gln Pro Thr Glu Ala Leu Ser Pro Glu Asp Gly Ala
-35
-30
-25

Ser Thr Ala Leu Ile Ala Val Val Ile Thr Val Val Phe Leu Thr Leu
-20 -15 -10

Leu Ser Val Val Ile Leu Ile Phe Phe Tyr Leu Tyr Lys Asn Lys Gly
-5 1 5 10

Ser Tyr Val Xaa Tyr Glu Pro Thr Glu Gly Glu Pro Ser Ala Ile Val
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Gln Met Glu Xaa Xaa Leu Ala Lys Gly Ser Glu 30

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-15 -10 -5

Asn Gln Ala Ser Leu Ile Ser Arg Cys Asp Leu Ala Gln Val Leu Gln

Leu Glu Asp Leu Asp Gly Phe Glu Gly Tyr Ser Leu Ser Asp Trp Leu 15 20 25 30

Cys Trp

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 Ile Phe Arg Gly Ile Arg His Gln Ile Tyr Leu Ile Arg Thr Leu Gln
 Ile Arg Gln Trp
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                                         -20
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Glu Leu Ala Xaa Thr Leu Ser Leu Thr Cys Ser Val Ser Gly Val Ser
                -10
                                    -5
 Ile Thr Ser Tyr Tyr Trp Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly
                            10
 Pro Glu Trp Ile Gly Xaa Ile Asp His Ser Gly Asp Thr Asp Tyr Asn
                       25
Pro Ser Leu Gln Ser Arg Val Thr Leu Ser Val Asp Thr Ser Lys Asn
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Gln Phe Ser Leu Arg Leu Leu Ser Val Ser Ala
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                                            -25
Thr Gly Val Thr Lys Val Ile Leu Pro Leu Phe Leu Cys Pro Leu Gly
                    -15
                                       -10
Met Val Glu Thr Ser Phe Gly
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Met Ser Tyr Val Val Thr Lys Thr Lys Ala Ile Asn Gly Lys Tyr His

Arg Phe Leu Gly Arg His Phe Pro Arg Phe Tyr Val Leu Tyr Thr Ile
-90 -85 -80

Phe Met Lys Gly Leu Gln Met Leu Trp Ala Asp Ala Lys Lys Ala Arg
-75 -70 -65

Arg Ile Lys Thr Asn Met Trp Lys His Asn Ile Lys Phe His Gln Leu
-60 -55 -50

Pro Tyr Arg Glu Met Glu His Leu Arg Gln Phe Arg Gln Asp Val Thr
-45 -30 -35

Lys Cys Leu Phe Leu Gly Ile Ile Ser Ile Pro Pro Phe Ala Asn Tyr
-25 -20 -15

Leu Val Phe Leu Leu Met Tyr Leu Phe Pro Arg Gln Leu Leu Ile Arg
-10 -5 1

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-10
-5

Cys Gln Phe Phe Pro His Asp Pro Ile Ser Ser Gln Tyr Ser Ser Pro 1 5 10

Gln Gly Lys Pro Cys Gln Val Thr Tyr Lys Phe Leu Phe Ile Leu Leu 15 20 25

Gly His Val Tyr Pro Arg Asp Gly Gly

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-70
-65

Gly Ala Gly Ala Val Ala Ala Pro Pro Ala Ile Asp Phe Pro Ala Glu
-60 -55 -50

Gly Pro Asp Pro Glu Tyr Asp Glu Ser Asp Val Pro Ala Xaa Ile Gln
-45 -40 -35

-45 -40 -35

Val Leu Lys Glu Pro Leu Gln Gln Pro Thr Phe Pro Phe Ala Val Ala
-30 -25 -20

Asn Gln Leu Leu Val Ser Leu Leu Glu His Leu Ser His Val His
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Glu

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 Ser Cys Arg His Leu
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                                -35
                                                   -30
 Thr Ala Gly Ser Ala Cys Ala Leu Ser Leu Leu Gln Phe Pro Val Leu
                            -20
                                                -15
 Ile Thr Gln Leu Cys Leu Gly Lys Gly Gln Ser Glu Pro Ile Gly Pro
                        - 5
                                         1
Leu Gln Asp Phe Val Ser Leu Glu Ser Thr Ser His Phe Tyr Ser Phe
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Thr Ser Ser Ser Leu Ser Trp Arg Met Gly Ser Gln Ile Arg Pro Ser
                1
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Val Cys Val Arg
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Ser Ser Ser Xaa Ala Cys Leu Trp Tyr Arg Pro Ile Ala Arg Arg Pro

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Ala Gly Pro Gly Gly Ser Leu Ser Ser Ala Gln Val His Pro Ala

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                         -20
                                             -15
 Trp Leu Leu Cys Arg Ile Cys Thr Phe Gly Phe His Gly Phe Ser Lys
                    - 5
 Tyr Thr Val Ser Arg Gly Thr Gln Gln Gly Ala Gly Xaa Xaa Xaa Gly
            10
                                 15
 Leu His Gln Asn Trp Glu Gln Trp Arg Gly Leu Val Gly Lys Ser Ser
                            30
 Ser Ala Ala Val Val Phe Cys Leu Thr Phe Asp Leu Val Thr Ser Phe
                        45
 Gln Leu Ala Ser Ala Ile Glu Ser Thr His Phe His Ala Gly Arg Asp
                    60
Gly Ser His Leu
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Met Glu Leu Ser Leu Pro Pro Ser Met Cys Asp Tyr Pro Xaa Phe Cys
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                                    -20
Leu Leu Leu Phe Pro Ala Ser Leu Arg Leu Leu Cys Val His Pro
                                 -5
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Met Asp Gln Lys Pro Leu Phe Thr Val Gly Cys Ala Gly Leu Ala Gly
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Ser Cys Arg Gly Ile Ser Phe Leu Arg Thr Arg
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                                 -15
                                                     -10
 Ile Gln Asp Leu Thr Met Ser Pro Thr Ala Gly Met Gln Trp His Asn
         -5
                            1
 His Gly Pro Pro Gln Ala Leu Pro Cys Pro Leu Arg Xaa
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 Met Ser Phe Leu Asn Val Asp Ile Thr Asp Cys Leu Tyr Asn Pro Ser
                    -40
                                        -35
 Val Cys Pro Val Ala Gln Ser Ser Leu Thr Cys Asp Phe Ile Asp Gly
                -25
                                    -20
 Ile Cys Leu Gly Ser Pro Leu Ala Glu Cys Leu Leu Gly Xaa Xaa Xaa
            -10
                                - 5
 Xaa Ile Xaa Gly Ile Asn Xaa Xaa Cys Phe Pro Cys Gly Val Lys Cys
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 Ala Gly Val Val Leu Gly Leu Ser Thr Leu Trp Tyr Val Val
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Met Lys Val Gly Lys Asp Ser Leu Glu Ser Leu Pro Ser Leu Cys Glu
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Lys His Ile Gly Pro Ser Gly Leu Phe Thr Phe Leu Ser Pro Ser Phe
                        -15
                                        -10
His Ser Val His Leu Ser Glu Leu Asn Glu Leu Tyr Thr Ile Ala Ala
· -5
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Gly
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Met Glu Ser Lys Val Leu Ile Ser Ala Ser Leu Leu Arg Ala Ser Gln
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Leu Lys Ile Lys Xaa Asn Lys Met Thr Asn Phe Leu Ile Leu
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Met Ala Ala Ser Val Leu Asn Thr Val Leu Arg Arg Leu Pro Met Leu
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Ser Leu Phe Arg Gly Ser His Xaa Xaa Phe Arg Phe Pro Ser Arg Leu
            - 5
Phe Ala Pro Lys Leu Pro Leu Arg Lys Ile Leu Cys Pro Gln Phe Pro
Phe Leu Leu Ile Arg Met Ser Pro Gly Asn Ile Trp Asn Gln Lys Asn
                    30
Thr Arg Ser Asp Met Val Leu Ala Pro Ser Gly Leu Thr Thr Ala Ala
                45
Thr Thr Arg Val Val Tyr Pro His Ser Gly Leu Gly Arg His Val Phe.
                                 65
Val Gly Ile Lys Leu Leu Gly Ile Pro Ala Pro Ser Val Glu Ile Thr
Ser Cys Met Leu Thr Leu
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Met Lys Ser Asn Leu Thr Leu Leu Thr Cys Leu Xaa Leu Xaa Gly Gly
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Glu Gly Trp Lys Gly Ala Ala Val Cys Phe Glu Thr Val Glu Gln Phe
Cys Ser Leu Arg Lys Trp His Val Thr Tyr Leu Xaa Lys Asp Ser Gly
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Leu Cys Gln Gln Gln Glu Lys Leu Tyr Thr Lys Phe Leu Val Cys Ile
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Lys Gly Ala Ser Asn Glu Glu Ile Lys Lys Thr Tyr
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 Met Leu Ala Ser Pro Cys Val Leu Val Gln Gly Ser Gly Xaa Ser Leu
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 Val Arg Thr Pro Trp Cys Pro Glu
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Met Asn Ile Ile Leu Glu Ile Leu Leu Leu Ile Thr Ile Ile Tyr
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                                                       -5
Ser Tyr Leu Glu Ser Leu Val Lys Phe Phe Ile Pro Gln Arg Arg Lys
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                                               10
Ser Val Ala Gly Glu Ile Val Leu Ile Thr Gly Ala Gly His
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Met Asp Leu Ile Gly Phe Gly Tyr Ala Ala Leu Val Thr Phe Gly Ser
               -35
                                   -30
                                                       -25
Ile Phe Gly Tyr Lys Xaa Arg Gly Gly Val Pro Ser Leu Ile Ala Gly
           -20
                               -15
                                                   -10
Leu Phe Val Gly Cys Leu Ala Gly Tyr Xaa Ala Tyr Arg Val Ser Asn
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Asp Lys Arg Asp Val
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Met Glu Gly Val Ala Xaa Xaa Thr Phe Leu Ala Ala Xaa Arg Arg Leu
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                                   -10
Val Thr Gly Gln Thr Ser Pro Arg Gly Thr Trp Cys Leu Tyr Pro Gly
                                               10
Phe Cys Arg Ser Val Ala Cys Ala Met Pro Cys Cys Ser His Arg Ser
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                       20
                                           25
Cys Arg Glu Asp Pro Gly Thr Ser Glu Ser Arg Glu Met Val Arg Val
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                                       40
Arg Asp His Gly
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WO 99/53051 605 <222> -21..-1 <400> 1381 Met Thr Gly Gln Phe Thr Lys Glu Ile Gly Leu Ile Gly Leu Thr Val -10 -15 Pro Cys Gly Trp Gly Ser Leu Ile Thr Met Ala Glu Gly Arg Glu Glu 5 Gln Val Thr Ser Gly . 15 <210> 1382 <211> 24 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -14..-1 <400> 1382 Met His Leu Gly Phe Ile Leu Ser Phe His Gly Leu Ile Ala Asn Phe -5 -10 Phe Phe Cys Leu Asn Ala Pro Ala 5 <210> 1383 <211> 26 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -20..-1 <400> 1383 Met Gly Arg Thr Arg Glu Ala Gly Cys Val Ala Ala Gly Val Val Ile -15 -20 Gly Ala Gly Ala Ala Thr Val Tyr Thr Asp 1 <210> 1384 <211> 60 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -38..-1 <400> 1384 Met Glu Ser His Ser Val Ala Gln Ala Arg Met Arg Xaa Xaa Asn Leu -30 -25 Ser Ser Leu Gln Pro Leu Pro Pro Gly Phe Lys Pro Xaa Ser Cys Leu -10 -15 -20 Ser Leu Leu Ser Asn Xaa Asp Tyr Arg His Ala Pro Pro Phe Leu Ala 1 Asn Phe Xaa Ile Phe His Arg Asp Gly Val Ser Pro

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Met Phe His Gly Ile Pro Ala Thr Pro Gly Ile Gly Ala Pro Gly Asn
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                                        -45
Lys Pro Glu Leu Tyr Glu Val Arg Gln His Gly Arg Ala Val Cys Gly
               -35
                                   -30
Gly Glu Asp Asn Ala Ser Pro Gly Glu Gly Leu His Gln Gly Leu Cys
          -20
                              -15
Leu Pro Gln Arg Val His Cys Ser Leu Leu Pro Ala Pro
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Met Pro His Ser Phe Val Ser Cys Asn Leu Phe Leu Ser Val Leu Asn
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                -15
Phe Leu Phe Leu Leu Ser Phe Ser Thr
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Met Ala Val Phe Leu Gln Lys Arg Lys His Thr Met Arg His His Leu
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Leu Leu Ser Thr Leu Ala Thr Ile Ala Gly Asn Ile Tyr Arg
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<210> 1388
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<212> PRT
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Met Ala Asp Ser Glu Ala Leu Pro Ser Leu Ala Gly Asp Pro Val Ala
                       -20
                                           -15
Val Glu Ala Leu Leu Arg Ala Val Phe Gly Val Val Val Asp Glu Ala
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                                       1
Ile Gln Lys Gly Thr Ser Val Ser Gln Lys Val Cys Xaa Trp Lys
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<400> 1389
Met Arg Leu Ala Met Val Gln Leu Val Leu Asn Asn Leu Lys Thr Phe
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                                           -25
Tyr Pro Phe Ala Asp His Asp Leu Ala Glu Leu Pro Val Ser Ser Pro
-20
                   -15
                                     -10
Leu Cys His Ala Val Leu Lys Thr Leu Gln Cys Trp Glu Gln Val Leu
Leu Arg Arg Leu Glu Ile His Gly Gly Pro Pro Gln Asn Tyr Ile Ala
                           20
                                               25
Ser His Thr Ala Xaa Xaa Ser Leu Ser Ala Gly Pro Ala Ile Leu Arg
                       35
                                           40
His Lys Ala Leu Leu Glu Pro
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<211> 51
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<400> 1390
Met Phe Lys Leu Phe Leu Phe Leu Phe Ile Leu Xaa Tyr Phe Xaa Xaa.
                   -15
                                       -10
                                                -5
Tyr Thr Leu Ser Ser Gly Ile Tyr Val Gln Asn Val Gln Val Cys Tyr
               1
                              5
Ile Gly Ile His Met Pro Trp Trp Phe Ala Ala Pro Met Asn Leu Ser
     15
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Ser Ala Leu
   30
<210> 1391
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<213> Homo sapiens
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<221> SIGNAL
<222> -21..-1
<400> 1391
Met Ile Tyr Ser Arg Ser Leu Glu Leu Ile Pro Leu Leu Ser Glu Ile
                      -15
                                          -10
Leu Tyr Ala Leu Ala Asn Ile Ser Pro Ile Pro Gln Thr
                   1
<210> 1392
<211> 18
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WO 99/53051 608 <222> -16..-1 <400> 1392 Met Val His Val Ile Phe Tyr Phe Val Leu Phe Leu Gly Ile Met Thr -10 Gln Arg <210> 1393 <211> 53 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -25..-1 <400> 1393 Met His Lys Phe Phe Arg His Phe Tyr Ser Asp Phe Leu Ile Tyr Phe -20 -15 Phe Gln Leu His Ser Cys Cys His Asp Lys Val Thr Ala Xaa Arg Ala - 5 7 Tyr Xaa His Tyr Ser Ser Leu Leu Thr Pro Tyr Leu Ser Gln His Pro 10 15 Cys Pro His Pro Gly 25 <210> 1394 <211> 121 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -26..-1 <400> 1394 Met Ala Ala Leu Gly Ser Pro Ser His Thr Phe Arg Gly Leu Leu Arg -20 -15 Glu Leu Arg Tyr Leu Ser Ala Ala Thr Gly His Pro Ile Ala Thr Pro <del>-</del> 5 Arg Pro Ile Gly Thr Xaa Val Lys Ala Phe Arg Ala His Arg Val Thr 10 . . 15 Ser Glu Lys Leu Cys Arg Ala Gln His Glu Leu His Phe Gln Ala Ala 30 Thr Tyr Leu Cys Leu Leu Arg Xaa Ser Gly Asn Met Trp Pro Tyr Ile 45 Arg Asn Phe Met Ala Arg Val Ser Ala Arg Trp Arg Ser Leu Leu Ala 60 Trp Trp Val Ser Ser Cys Pro Ile Ser Leu Glu Gly Arg Ala Gly Ser 75 His Glu His Gly Glu Tyr Pro Trp Met 90 <210> 1395 <211> 30

<212> PRT <213> Homo sapiens <220> <221> SIGNAL

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   Met Ile Thr Asp Val Gln Leu Ala Ile Phe Ala Asn Met Leu Gly Val
      -25
                                  -20
                                             -15
   Ser Leu Phe Leu Leu Val Val Leu Tyr His Tyr Ala Ala Val
                              -5
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   <211> 25
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   Met Ala Glu Gly Ala Leu Ser Phe Leu Cys Ser Leu Ser Gln Asn Ala
       -15
                      -10
   Leu Asn Ile Ser Leu Ile Ser Arg Lys
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  Met Tyr Pro Ser Phe Leu Leu Cys Phe Thr Leu Val Gly Thr Gln Leu
   -15
                        -10
  Arg Asn Ser Ser Leu Ala Met
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 Met Glu Ser Cys Thr Val Gly Cys Ala Thr Ala Ser Ser Trp Gly Cys
 -15
                   -10
 Thr Ser Arg
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 Met Ala Met Ser Phe Glu Trp Pro Trp Gln Tyr Arg Phe Pro Pro Phe
                               -35
                                                  -30
 Phe Thr Leu Gln Pro Asn Val Asp Thr Arg Gln Lys Gln Leu Ala Ala
```

```
-25
                            -20
                                                -15
 Trp Cys Ser Leu Val Leu Ser Phe Cys Arg Leu His Lys Gln Ser Ser
    -10 .
              -5
                                            1
 Met Thr Val Met Glu Ala Gln Glu Ser Pro Leu Phe Asn Asn Val Lys
                10
 Leu Gln Arg Lys Leu Pro Val
            25
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 Met Arg Leu His Val His Ser Leu Ser Pro Phe Ser Phe Ala Cys Leu
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 Pro Phe Leu Ser Pro Pro Leu
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 <222> -26..-1
<400> 1401
Met Leu His Phe Xaa Tyr Met Ile Xaa Val Cys Leu Glu Arg Met Cys
               -20
                                          -15
Ile Leu Gln Leu Leu Ser Ala Val Leu Tyr Arg Phe
-10
                   - 5
<210> 1402
<211> 35
<212> PRT
<213> Homo sapiens
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<221> SIGNAL
<222> -30..-1
<400> 1402
Met Ser Ser Glu Pro Pro Pro Pro Pro Gln Pro Pro Thr His Gln Ala
                  -25
                          -20
Ser Val Gly Leu Leu Asp Thr Pro Leu Gly Ala Val Ser Ala His His
Pro Leu Cys
       5
<210> 1403
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<212> PRT
<213> Homo sapiens
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<221> SIGNAL
<222> -20..-1
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  Met Phe Leu Asp His Val Arg Phe Leu Thr Ser Ile Ser Phe Leu Ala
                  -15
                                  -10
  Leu Val Leu Trp Asn Val Phe Leu Asn Ser Thr Arg Leu
                  1. .
                                 5
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  <211> 26
  <212> PRT
  <213> Homo sapiens
  <220>
  <221> SIGNAL
  <222> -19..-1
  <400> 1404
  Met Arg Glu Lys Pro Gln Pro Ala Leu Leu Thr Ser Ser Glu Leu Pro
                -15
                                    -10
  Ala Leu Ala Ser Gln Ile His Cys Arg Val
              1
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  <211> 38
  <212> PRT
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  <222> -26..-1
  <400> 1405
 Met Pro His Asn His Leu Glu Gly Asp Ala Leu Leu Arg Val Pro Val
    -25 -20
                                            -15
 Leu Cys Ile Trp Arg Ala Trp Leu Arg Ala Glu Val Gly Gly Arg Ala
                     -5
 Pro Leu Pro Gly Arg Met
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 <222> -22..-1
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 Met Lys Asn Thr Leu Tyr Tyr Asn Phe Cys Leu Phe Trp Ile Xaa Leu
                            -15
 Pro Pro His Thr Cys Thr His Thr Asp Thr His
   -5
                        1
 <210> 1407
 <211> 53
 <212> PRT
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612
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   Met Cys Leu Asn Pro Ala Cys Ser Gly Pro Leu Ser Leu Arg Ser Pro
                      -30
                                          -25
   Arg Leu Pro Pro Leu Phe Cys Thr Phe Leu Ser Leu Ser Leu His Pro
                  -15
  Trp Gly Gly Phe Phe Leu Cys Ala Trp Ile Ser Xaa Phe Leu Pro Trp
                                       -10
  Val Cys Val Xaa Ala
  . 15
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  <221> SIGNAL
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  Met Ala His Ser Lys Thr Arg Thr Asn Asp Gly Lys Ile Thr Tyr Pro'
                                      -80
  Pro Gly Val Lys Glu Ile Ser Asp Lys Ile Ser Lys Glu Glu Met Val
              -70 ·
                                 -65
  Arg Arg Leu Lys Met Val Val Lys Thr Phe Met Asp Met Asp Gln Asp
                             -50
 Ser Glu Glu Lys Glu Leu Tyr Leu Asn Leu Ala Leu His Leu Ala
                                                  -45
                         -35
 Ser Asp Phe Phe Leu Lys His Pro Asp Lys Asp Val Arg Leu Leu Val
                     -20
                                         -15
 Ala Cys Cys Leu Ala Asp Ile Phe Arg Ile Tyr Ala Pro Glu Ala Pro
                 -5
 Tyr Thr Ser Pro Lys
        10
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 <221> SIGNAL
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 <400> 1409
Met Xaa Ser Cys Glu Ile Ala Trp Thr Ala Thr Pro Ser Ser Ala Ala
                                -10
Phe Ala Gln Ala Phe Pro Thr Ala Cys Asn
        1
<210> 1410
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<221> SIGNAL
<222> -25..-1 ...
<400> 1410
Met Cys His Tyr Leu Trp Lys Lys Leu Tyr Ser Thr Leu Leu Tyr Ile
                    -20
                                        -15
Leu Ser Arg Ser Ser Gly Arg Arg Gly Lys Asn Leu Ile Thr Ala Val
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- 5
 Ala Ser Arg Ala Gly Asn Leu Gly Val Trp Thr Glu Lys Gly
                              15
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 <213> Homo sapiens
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 <222> -27..-1
 <400> 1411
Met Xaa Ser His Arg Leu Phe Gly Cys Phe Pro Ser Asp Leu Ser Arg
        -25
                             -20
                                                  -15
Met Val Leu Leu Ser Ser Ala Leu Leu Ser Thr Glu Asn
                     -5
<210> 1412
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<212> PRT
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<222> -21..-1
<400> 1412
Met Arg Pro Ser His Ser Ser Ala Tyr Leu Cys Leu His Leu Cys Ala
    -20
                         -15
                                             -10
Phe Ser Thr Glu Gly Trp Met Asn Arg Leu Ser Ser Ser Leu Arg Leu
                                     5
Ala Pro Leu Pro Leu Tyr Pro Phe Cys Leu Pro Ser Asn Ser Pro
            15
                                 20
<210> 1413
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<400> 1413
Met Trp Ser Arg Leu Val Trp Leu Gly Leu Arg Ala Pro Leu Gly Gly
                        -10
Arg Gln Gly Phe Thr Ser Lys Ala Asp Pro Gln Gly Ser Gly Arg Ile
Thr Ala Ala Val Ile Glu His Leu Glu Arg Leu Ala Leu Val Asp Phe
           20
                                25
Gly Ser Arg Glu Ala Val Ala Arg Leu Glu Lys Ala Ile Ala Phe Ala
Asp Arg Leu Arg Ala Val Asp Thr Asp Gly Val Glu Pro Met Glu Ser
                        55
Val Leu Glu Asp Arg Cys Leu Tyr Leu Arg Ser Asp Asn Val Val Glu
                    70
                                        75
Gly Asn Cys Ala Asp Glu Leu Leu Gln Asn Ser His Arg Val Val Glu
                85
Glu Tyr Phe Val Ala Pro Pro Gly Asn Ile Ser
           100
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WO 99/53051
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 Met Ala Pro Pro Val Arg Tyr Cys Ile Pro Gly Glu Arg Leu Cys Asn
                          -75
                                              -70
 Leu Glu Glu Gly Ser Pro Gly Ser Gly Thr Tyr Thr Arg His Gly Tyr
                     -60
                                          -55
                                                               -50
 Ile Phe Ser Ser Leu Xaa Gly Cys Leu Met Lys Ser Ser Glu Asn Gly
                 -45
                                      -40
 Ala Leu Pro Val Val Ser Val Val Arg Glu Thr Glu Ser Gln Leu Leu
             -30
                                 -25
 Pro Asp Val Gly Ala Ile Val Thr Cys Lys Ser Leu Ala Ser Ile His
        -15
                             -10
 Ala Leu Pro
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 <222> -60..-1
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Met Val Gly Asn Gln Gly Pro Gln Pro Pro Pro Phe Pro Met Glu Pro
                    -55
                                         -50
Thr Met Ala Gln Tyr Gln Ala Ile Ser Lys His Leu Pro Lys Val Cys
                                    -35
Gln Glu Pro His Leu Pro Arg Gly His Leu Gln Pro Gln Gln His Arg
             -25
                                -20
Leu Leu Val Ala Arg Leu His Met Ala Ser Leu Ala Arg Arg Cys Thr
                            - 5
Glu Trp Ala Lys Leu His Cys Ser Asp Ala Arg Leu Pro Trp Val Ser
                    10
<210> 1416
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<222> -28..-1
<400> 1416
Met Lys Pro Gln Thr Leu Ala Val Ser Val Thr Val Leu Lys Asp Gly
         -25
                                -20
                                                     -15
Val Ala Gly Val Cys Phe Phe Arg Arg Ser Asp Ala Ser Glu Val Ser
       -10
Ser Phe Trp
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<221> SIGNAL <222> -48..-1

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<222> -43..-1
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Met Val Val Leu Ile Cys Leu Ser Leu Met Ile Ser Asn Thr Glu Leu
            -40
                                 -35
Phe Phe Ile Arg Phe Leu Thr Ala Cys Met Pro Ser Phe Glu Lys Cys
 -25
                             -20
Leu Phe Leu Ser Phe Ala His Phe Leu Met Gly Arg Thr His Arg
<210> 1418
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<212> PRT
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<222> -22..-1
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Met Ser Ser Leu Tyr Ile Leu Asp Ile Ser Leu Leu Ser Asp Ile Leu
                            -15
                                                -10
Phe Ala Asn Ile Phe Ser His Ser Trp Asp Val Phe Pro Leu Ser Phe
                        1
                                        5
Leu Phe Phe Ser
<210> 1419
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<222> -84..-1
<400> 1419
Met Gly Gln Gly Ala Arg Gly Trp His Arg Glu Pro Gly Leu Gly Leu
                                    -75
Arg His Ser Pro Arg Arg Leu Ser Gly Ala Leu His Leu Glu Ala Gly
            -65
                               -60
Cys Asp Arg Asn Ala Thr Thr Val Arg Pro Leu Arg Ala Lys Xaa Gly
       -50
                            -45
Asp Ala Leu Pro Glu Glu Ile Arg Glu Pro Ala Leu Arg Asp Ala Gln
                        -30
Trp Val Arg Asp Gln Leu Ala Ser Ser Leu Leu Ile Ile Leu Leu Pro
                   -15
                                       -10
Asn Thr Gln Asp Leu Arg Ile Gln Lys Asp Pro Thr Pro Gly Pro
                                5
<210> 1420
<211> 87
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616
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 Met Arg Lys Arg Lys Ile Ser Val Cys Gln Gln Thr Trp Ala Leu Leu
             -45
                                  -40
 Cys Lys Asn Phe Leu Lys Lys Trp Arg Met Lys Arg Glu Ser Leu Met
       -30
                             -25
                                                  -20
 Glu Trp Leu Asn Ser Leu Leu Leu Leu Cys Leu Tyr Ile Tyr Pro
     -15
                         -10
                                             -5
 His Ser His Gln Val Asn Xaa Xaa Ser Ser Leu Leu Thr Met Asp Leu
                 5 '
                                     10
 Gly Arg Val Asp Xaa Xaa Asn Glu Ser Arg Phe Ser Val Val Tyr Thr
 Pro Val Thr Asn Thr Thr Pro
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 <400> 1421
Met Cys Thr Cys Leu Cys Val Cys Leu Tyr Met Tyr Asn Met Gln Phe
                    -25
                                 -20
Leu Xaa Phe Val Phe Val Cys Xaa Leu Leu Lys Cys Met Ser Val Pro
                -10
<210> 1422
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<222> -31..-1
<400> 1422
Met Ala Ala Ser Ala Ala Ala Glu Leu Gln Ala Ser Gly Gly Pro
    -30
                        -25
Arg His Pro Val Cys Leu Leu Val Leu Gly Met Ala Gly Ser Gly Lys
                    -10
                                        -5
Thr Thr Phe Val Gln Arg Leu Thr Gly His Leu His Ala Gln Gly Thr
Pro Pro Tyr Val Ile Asn Leu Asp Pro Ala Val His Glu Val Pro Xaa
                           25
Pro Ala Asn Ile Asp Ile Arg Asp Thr Val Lys Tyr Lys Glu Val Met
Lys Gln Tyr Gly Leu Gly Pro Asn Gly Gly Ile Val Thr Ser Leu Asn
Leu Phe Xaa Thr Arg Phe Asp Gln Val Met Lys Leu Leu Arg Arg Pro
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Arg Thr Cys Pro Asn Met Cys
<210> 1423
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<220>

<213> Homo sapiens

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  <222> -20..-1
  <400> 1423
  Met Tyr Ala Cys Ala Met Leu Val Leu Leu Thr His Gly Leu Ile His
                     -15
                                      -10
 Tyr Ser Phe Thr His His Leu His Tyr Val Phe Ile Leu Ile Leu Pro
                 1
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  Leu Pro Pro Pro Pro Gln
   . 15
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 <222> -24..-1
 <400> 1424
 Met Gly Phe Leu Gly Ser Pro Arg Gln Arg Asn Ser Met Cys Leu Leu
                -20
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 Leu Asp Val Ser Ser Xaa Lys Ser Thr Asp Asn Xaa Xaa Xaa Xaa Xaa
                                 1
 Leu Ile Ile Tyr Tyr Leu Ile Thr Arg Lys Gly Pro Gly
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Met Ser Cys Gln Xaa Xaa Leu Ala Xaa Thr Leu Thr Trp Leu Met Ile
            -40
                                -35
Arg Gly Arg His Pro Tyr Leu Thr Arg Arg Ser Ala Arg Asn Phe Asn
                            -20
                                                -15
Ile Phe Leu Ala Ala Pro Ser Pro Val Trp Gln Pro Gln Arg Thr Arg
   -10
Arg Pro Gln
<210> 1426
<211> 51
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<222> -34..-1
<400> 1426
Met Cys Pro Ala Trp Leu Pro Cys Trp Thr Ala Gln Thr Glu His Leu
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                                   -25
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Asp Arg Tyr Arg Lys Phe His Gln Met Ala Leu Xaa Pro Gly Thr Ser -15 -10 - 5 Arg Ala Gln Ala Leu Leu Tyr Asn Glu Val Leu Glu Arg Phe Met Phe 1 Thr Arg Leu

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 Met Asn Val Met Lys Arg Ile Cys Thr Phe Leu Leu Pro Ser His Ser
             -15
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 Thr Ser Gly Pro Leu Cys Cys Ser Asn Ala His Leu Pro Ala Thr Ser
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 Ser Thr Leu Lys His Cys Arg Ala Trp Arg Glu Ala
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Met Val Val Phe Gly Tyr Glu Ala Gly Thr Lys Pro Arg Asp Ser Gly
                        -115
                                             -110
Val Val Pro Val Gly Thr Glu Glu Ala Pro Lys Val Phe Lys Met Ala
-105
                    -100
                                        -95
Ala Ser Met His Gly Gln Pro Ser Pro Ser Leu Glu Asp Ala Lys Leu
                -85
                                    -80
Arg Arg Pro Met Val Ile Glu Ile Glu Lys Asn Phe Asp Tyr Leu
            -70
                                 -65
Arg Lys Glu Met Thr Gln Asn Ile Tyr Gln Met Ala Thr Phe Gly Thr
                            -50
Thr Ala Gly Phe Ser Gly Ile Phe Ser Asn Phe Leu Phe Arg Arg Cys
                        -35
                                            -30
Phe Lys Val Lys His Asp Ala Leu Lys Thr Tyr Ala Ser Leu Ala Thr
-25
                    -20
                                        -15
Leu Pro Phe Leu Ser Thr Val Val Thr Asp Lys Leu Phe Val Ile Asp
               -5
Ala Leu Tyr Ser Asp Asn Ile Ser Lys Glu Asn Cys Val Phe Arg Ser
        10
                            15
Ser Leu Ile Gly Ile Val Cys Gly Val Phe Tyr Pro Ser Ser Xaa Ala
Phe Thr
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<222> -38..-1
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<400> 1429

Met Ala Glu Ile Thr Asn Ile Arg Pro Ser Phe Asp Val Ser Pro Val

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-35
                                -30
                                                    -25
 Val Ala Gly Leu Ile Gly Ala Ser Val Leu Val Val Cys Val Ser Val
         -20
                             -15
                                                -10
 Thr Val Phe Val Trp Ser Cys Cys Xaa Gln Gln Ala Glu Lys Lys His
                        1
                                     5
 Lys Asn Pro Pro Tyr Lys Phe Ile His Met Leu Lys Gly Xaa Ser
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 Met Val Ile Leu Thr Met Leu Ile Leu Leu Ile His Glu His Gly Ile
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 Phe Phe Ser Leu Val Cys Val Leu Phe
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 <211> 33
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 <213> Homo sapiens
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 <222> -29..-1
<400> 1431
Met Phe Ser His Asn His Ser Tyr Thr Tyr Thr Pro Gln His Ser Pro
         -25 -20
Leu Thr His Thr His Thr Cys Thr Pro Pro Ser Thr Ala His Pro Arg
                               -5
Gly
<210> 1432
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<400> 1432
Met Phe Xaa Met Ile Leu Leu Cys Phe Leu Ala Val Ser Asn Phe Asn
                 -10
                                      -5 <sup>`</sup>
Lys Leu Leu Trp Gly Xaa
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<211> 31
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 Met Phe Leu Ile Leu Gly Lys Phe Ser Arg Val Met Gly Leu Pro Leu
 -25 -20
 Ala Cys Phe Ser Leu Phe Gly Xaa Leu Pro Gln Gly Leu Leu Ile
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 <222> -19..-1
 <400> 1434
 Met Val Ala Leu Gly Gln Leu Ala Xaa Leu Pro Gly Xaa Xaa His Gly
               -15
                                   -10
 Gly Leu Ser Ala Val Thr Val Val Leu Pro Ile Leu Leu Cys
            1
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Met Pro Val Ser Phe Val Cys Leu Leu Phe Arg Asn Val Tyr Ser Asn
-15 -10
Leu Leu Pro Ser Phe Phe
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<210> 1436
<211> 64
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<222> -27..-1
Met Gly Ser Gly Gly Asp Ser Leu Leu Gly Gly Arg Gly Ser Leu Pro
       -25
                          -20
                                             -15
Leu Leu Pro Ala His His Gly Arg His Gly Ser Gly Leu Pro Ala
   -10
                       -5
Pro Asp Pro Ser Pro Pro Pro Gly Pro Ala Val Pro Gly Pro Trp Pro
              10
                                  15
Cys Gln Asp Glu Leu Pro Ser Leu Arg Pro Ala Thr Ser His His Phe
                              30
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  Met Ala Val Gly Gly Thr Ala Val Ile Thr Arg Arg Leu Leu Gly Arg
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                                          -15
  Ser Gly Phe Ser Phe Gln Val Ser Gly Trp Gly Trp Gly Glu Arg Val
                  -5
  Asp Asp Phe Leu Phe Ser Ser Gly Ile Asp Gly
          10
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  <222> -21..-1
  <400> 1438
 Met Arg His His Val Arg Xaa Pro Ala Leu Ser Ser Leu Ala His His
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                                              -10
 Pro Arg Thr Ser Gly Gln Lys Arg Glu Pro Ile Ala Pro Ala Gln Leu
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 Ser Pro
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 <400> 1439
 Met Leu Ile Leu Asn Gly Phe Arg Gly His Ala Thr Asp Ser Val Lys
                                  -65
 Asn Ser Met Glu Ser Met Asn Thr Asp Met Val Ile Ile Pro Gly Gly
                             -50
                                                 -45
 Leu Thr Ser Gln Leu Gln Val Leu Asp Val Val Tyr Lys Pro Leu
                         -35
                                             -30
 Asn Asp Ser Val Arg Ala Gln Tyr Ser Asn Trp Leu Leu Ala Gly Asn
                     -20
                                         -15
 Leu Ala Leu Ser Pro Thr Gly Asn Ala Lys Lys Pro Pro Leu Gly Leu
                 -5
                                     1
 Phe Leu Glu Trp Val Met Val Ala Trp Asn Ser Ile Ser Ser Glu Ser
                             15
 Ile Val Gln Gly Xaa Lys Glu Val Pro Tyr Leu Xaa Gln Leu Gly Gly
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 Gly Arg Arg
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Met Ile Cys Thr Thr Val Tyr Ile Thr Met Ala Pro Tyr Cys Leu Ser
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Asn Cys Leu Leu Xaa Xaa Ser Trp Gly Leu His Leu Tyr Arg Phe Leu

-5

1

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Ala Pro

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Met Val Ser Leu Cys Val Ala Ala Leu Phe Pro Leu Gln Ala Tyr Gly

<210> 1442

<211> 28

<212> PRT

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<222> -24..-1

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Met Leu Ser Ile Phe Ser Phe Phe Cys Arg Pro Phe Val Tyr Leu Leu
-20 -15 -10

Leu Arg Asn Leu Xaa Ser Tyr Ser Leu Pro Thr Thr

<210> 1443

<211> 94

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<222> -77..-1

<400> 1443

Met Phe Pro Val Ser Ser Gly Cys Phe Gln Glu Gln Gln Glu Thr Asn
-75 -70 -65

Lys Ser Leu Pro Arg Ser Ala Ser Thr Pro Glu Thr Arg Thr Lys Phe
-60 -55 -50

Thr Gln Asp Asn Leu Cys Xaa Ala Gln Arg Glu Arg Leu Asp Ser Ala
-45 -35 -30

Asn Leu Trp Val Leu Val Asp Cys Ile Leu Arg Asp Thr Ser Glu Asp
-25
-20
-15

Leu Gly Leu Gln Cys Asp Ala Val Asn Leu Ala Phe Gly Arg Arg Cys

Glu Glu Leu Glu Asp Ala Arg His Lys Leu Gln Xaa His Leu
5 10 15

<210> 1444

<211> 20

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623
  <222> -15..-1
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 Met Pro Leu Val His Ser Phe Leu Trp Leu Ser Ser Ile Leu Tyr Ile
                     -10
                                          -5
 Tyr His Leu Arg
 <210> 1445
 <211> 56
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 <213> Homo sapiens
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 <222> -24..-1
 <400> 1445
 Met Ile Ser Asn Gly Lys Phe Phe Cys Phe Phe Xaa Val Phe Xaa Phe
                 -20
                                     -15
 Xaa Phe Leu Xaa Arg Xaa Leu Xaa Xaa Xaa Pro Arg Leu Glu Cys Asn
             -5
                                 1
 Gly Lys Xaa Ser Ala His Xaa Asn Leu Arg Leu Leu Ser Xaa Ser Asn
                         15
 Ser Leu Ala Ser Ala Pro Arg Gly
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Met Glu Asp Ser Ala Ser Ala Ser Leu Ser Ser Ala Ala Ala Thr Gly
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                     -85
                                         -80
Thr Ser Thr Ser Thr Pro Ala Ala Pro Thr Ala Arg Lys Gln Leu Asp
                 -70
                                     -65
Lys Glu Gln Val Arg Lys Ala Val Asp Ala Leu Leu Thr His Cys Lys
             -55
                                 -50
 Ser Arg Lys Asn Asn Tyr Gly Leu Leu Leu Asn Glu Asn Glu Ser Leu
                          . -35
                                                 -30
 Phe Leu Met Val Val Leu Trp Lys Ile Pro Ser Lys Glu Leu Arg Val
                         -20
                                            -15
Arg Leu Thr Leu Pro His Ser Ile Arg Ser Asp Ser Glu Asp Ile Cys
-10
                                         1
Xaa Phe Thr Lys Asp
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<211> 59
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<222> -29..-1
<400> 1447
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Met Asn Ala Glu Gly Ala Ser Pro Gly Lys Glu Thr Asn Thr Gly Thr

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624
                 -25
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  Leu Ile Glu Leu Asn Leu Xaa Ser Pro Val Ala Leu Gln Trp Pro Leu
             -10
                                  <del>-</del> 5
  Ser Ser Pro Ser Cys Leu Arg Ile Leu Ser Asn Lys Val Pro Arg Asn
                         10
  Leu Arg Trp Gln Lys His Tyr Ser Thr His Gln
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 <400> 1448
 Met Leu Gly Leu Asp Glu Leu Gly Arg Ser Gly Cys Gly His Cys Thr
             -60
                                 -55
                                                      -50
 Gln Ala Asp Leu Arg Phe Gly Asp Ala Ala Gly Xaa Glu Pro Arg Xaa'
        -45
                             -40
                                                 -35
 Arg Xaa Thr His Arg Asn Thr Ala Ala Ala Arg Val Pro Pro Pro Pro
    -30
                         -25
                                             -20
 Arg Val Met Ala Ala Ala Ala Leu Arg Ala Pro Ala Gln Ser Ser
            -10
                                         -5
 Val Thr Phe Glu Asp Val Ala Val Asn Phe Ser Leu Glu Glu Trp Ser
            5
                                 10
 Leu
 <210> 1449
 <211> 49
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 <213> Homo sapiens
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<222> -26..-1
<400> 1449
Met Ser Ala Leu Lys Asp Phe Arg Glu Phe Leu Asn Trp Trp Gly Asn
                        -20
Leu Ser Phe His Leu Gln Glu Ala His Gly Ser Glu Ile Ala Glu Met
                    -5
Gly Ala Gly Ile Leu Glu Glu Lys Asn Tyr Gly Gln Gln Xaa His Cys
            10
                                15
Asn
<210> 1450
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<213> Homo sapiens
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<222> -30..-1
<400> 1450
Met Ser Leu Pro Pro Phe Phe His Pro Ser Pro Ala Pro Ser Leu Ala
-30
                    -25
                                       -20
Pro Pro Pro Ser Leu Phe Leu Ser Leu Pro Pro Ser Leu Ser Pro Pro
                                    -5
Leu Pro Ala Arq
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<222> -25..-1

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<210> 1451
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<222> -13..-1
<400> 1451
Met Phe Phe Leu Cys Gly Phe Leu Tyr Leu Cys Phe Ile Ser Phe Phe
Phe Phe
  5
<210> 1452
<211> 51
<212> PRT
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<222> -42..-1
<400> 1452
Met Lys Ala Gly Pro Cys Ser Cys Gln Glu Gly Gly Arg Gln Trp Ala
        -40
                            -35
His Gly Ser Val Pro Leu Gln Pro Thr Ala Arg Leu Ala Ala Leu Gly
-25
                        -20
                                             -15
Ile Phe Leu Cys Pro Gly Glu Thr Leu Ser Ala Ser Leu His Trp Asn
-10
                    -5
Pro Ile Gly
<210> 1453
<211> 53
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<222> -23..-1
<400> 1453
Met Leu Ser Gln Ser Phe Gln Lys Asn Lys Thr Asn Leu Leu Cys Leu
           -20
                                -15
                                                    -10
Thr Phe Gln Arg Cys Gln Ser Tyr Asn Trp Leu Asn Ile Phe Glu Ala
      -5
                            1
                                            5
Thr Tyr Met Thr Thr Leu Phe Ile Ser Val Ile Xaa Thr Asn Phe Leu
                                        20
Lys Arg Tyr Leu Leu
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<400> 1454
 Met Phe Leu Phe Cys Trp Glu Lys Ser Pro Arg Met Gln Leu Leu Gly
 -25
                  -20
                                          -15
 Cys Met Val Leu Tyr Asp Cys Phe Ser Phe Lys Lys Leu Pro Gly
                  - 5
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 <211> 47
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 <213> Homo sapiens
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 <222> -30..-1
 <400> 1455
 Met Ser Phe Ile Ser Val Ile Phe Pro Leu Ile Leu Leu Asn Arg Phe
                     -25
                                         -20
 Ser Phe Val Cys Phe Phe His Val Phe Tyr Cys Val Phe Cys Asn Val
                 -10
                                      -5
 Ser Ser Leu Phe Ser Tyr Gln Phe Leu Leu His Phe Cys Asp Asp
         5
                             10
 <210> 1456
 <211> 35
 <212> PRT
<213> Homo sapiens
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 <222> -31..-1
<400> 1456
Met His Glu Tyr Leu Pro Arg Asn Phe His Asp Phe Asn Ser Pro Asn
                       - 25
                                             -20
Ser Lys Leu Gly Met Gly Met Gly Phe Phe Ser Gly Val Lys Ser Trp
                    -10
                                         -5
Ile Gly Gly
<210> 1457
<211> 83
<212> PRT
<213> Homo sapiens
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<221> SIGNAL
<222> -36..-1
<400> 1457
Met Ala Ser Xaa Val Pro Val Lys Asp Lys Lys Leu Leu Glu Val Lys
                        -30
                                            -25
Leu Gly Glu Leu Pro Ser Trp Ile Leu Met Arg Asp Phe Ser Pro Ser
                    -15
                                        -10
Gly Ile Phe Gly Ala Phe Gln Arg Gly Tyr Tyr Arg Tyr Tyr Asn Lys
Tyr Ile Asn Val Lys Lys Gly Ser Ile Ser Gly Ile Thr Met Val Leu
                            20
Ala Cys Tyr Val Leu Phe Ser Tyr Ser Phe Ser Tyr Lys His Leu Lys
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                        35
His Glu Ser
45
<210> 1458
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<211> 24
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<222> -18..-1
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Met Val Ile Ser Ala Gly Ala Leu Leu Trp Met Ala Trp Asp Gly Gln
            -15
                                -10
Leu Ser Arg Pro Glu Gly Ala Arg
  1
<210> 1459
<211> 31
<212> PRT
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<400> 1459
Met Val His Cys Asn Leu Glu Leu Leu Gly Ser Ser Tyr Asn Pro Ile
           -15
                                -10
                                                    -5
Ser Ala Ser Pro Val Ala Arg Thr Ile Ser Cys Pro Ala Ile Val
        1
                      5
<210> 1460
<211> 127
<212> PRT
<213> Homo sapiens
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<400> 1460
Met Leu Gly Ser Gly Phe Lys Ala Glu Arg Leu Arg Val Asn Leu Arg
           -85
                                -80
                                                    -75
Leu Val Ile Asn Arg Leu Lys Leu Leu Glu Lys Lys Lys Thr Glu Leu
       -70
                            -65
                                                -60
Ala Gln Lys Ala Arg Lys Glu Ile Ala Asp Tyr Leu Ala Ala Gly Lys
                        -50
                                            -45
Asp Glu Arg Ala Arg Ile Arg Val Glu His Ile Ile Arg Glu Asp Tyr
                   -35
                                        -30
Leu Val Glu Ala Met Glu Ile Leu Glu Leu Tyr Cys Asp Leu Leu
               -20
                                    -15
Ala Arg Phe Gly Leu Ile Gln Ser Met Lys Glu Leu Asp Ser Gly Leu
           -5
Ala Glu Ser Val Ser Thr Leu Ile Trp Ala Ala Pro Arg Leu Gln Ser
                       15
Glu Val Ala Glu Leu Lys Ile Val Ala Asp Gln Leu Cys Pro Ser
                   30
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<211> 54
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<213> Homo sapiens
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<222> -43..-1
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<400> 1461

Met Arg Gly Trp Xaa Ala Pro Ala Trp Arg Xaa Leu Xaa Thr Arg Arg
-40 -35 -30

Leu Pro Met Gly Ser Arg His Gly Ala Ser Pro Ala Ser Ala Val Trp
-25 -20 -15

Cys Leu Xaa Leu Lys Leu Val Pro Ala Leu Cys Ile Ser Gly Leu Thr
-10 -5 1 5

Leu Gly Ile Gln Gly Phe

10

<210> 1462

<211> 49

<212> PRT

<213> Homo sapiens

<220>

<221> SIGNAL

<222> -34..-1

<400> 1462

Met Tyr Phe Lys Thr Thr Thr Xaa Xaa His Ser Ala His Met Leu Leu -30 -25 -20

Gln Ile Cys Phe Phe Arg Leu Thr Ile Leu Xaa Phe His Asp Asn Thr
-15 -10 -5

Trp Gly Ser Thr Ser Phe Ser Xaa Val Ala Ala Met Leu Phe His Tyr

1 5 10

Arg

15

<210> 1463

<211> 26

<212> PRT

<213> Homo sapiens

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<221> SIGNAL

<222> -24..-1

<400> 1463

Met Ser Ser Asn Ile Gln Arg Leu Gly Phe Pro Leu Leu Phe Leu Phe -20 -15 -10

Phe Leu Phe Phe Phe Phe Phe Phe -5

<210> 1464

<211> 69

<212> PRT

<213> Homo sapiens

<220>

<221> SIGNAL

<222> -67..-1

<400> 1464

Met Cys Asp Ala Phe Val Gly Thr Trp Lys Leu Val Ser Ser Glu Asn -65 -55

Phe Asp Asp Tyr Met Lys Glu Val Gly Val Gly Phe Ala Thr Arg Lys
-50 -45 -40

Val Ala Gly Met Ala Lys Pro Asn Met Ile Ile Ser Val Asn Gly Asp
-35 -25 -20

Val Ile Thr Ile Pro His Leu Val Leu Pro Leu Pro Met Leu Pro Thr

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WO 99/53051
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                 -15
                                      -10
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 Ser Asn Arg Lys Arg
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 <222> -21..-1
 <400> 1465
 Met Phe Leu Tyr Arg Ser Phe Gly Gly Gln Leu Leu Ser Phe Leu Leu
                         -15
                                              -10
 Gly Thr Tyr Leu Gly Arg Arg Glu Val Ala Gly Pro Gln His Gly Gln
 -5
                     1
 Phe Ser Lys
 <210> 1466
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 <222> -16..-1
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 Met Xaa Gly Phe Phe Cys Leu Cys Ala Phe Asn Ser Phe Leu Leu Ser
   -15
                         -10
 Pro Glu Gly
 <210> 1467
 <211> 68
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 <222> -66..-1
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 Met Ile Phe Pro His Cys Met Tyr Cys Leu Glu Cys Ile Thr Lys Asn
                        -60
                                             -55
 Gly Leu Leu Gly Leu Lys Val Leu Pro Leu Tyr Gly Ile Met Leu Ile
                    -45
                                         -40
 Phe Phe Pro Lys Val Val Tyr Asn Asn Gln Pro Leu His Tyr Lys Ser
                -30
                                    ~25
 Val Met Val Phe Gln Leu Thr Ser Phe Leu Ser Ile Xaa Ile Phe Val
           -15
 Asn Pro Thr Arg
       1
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<220> <221> SIGNAL <222> -54..-1

<400> 1468

Met Val Ser Met Ser Phe Lys Arg Asn Arg Ser Asp Arg Phe Tyr Ser

-50

-45

Thr Arg Cys Cys Gly Cys Cys His Val Arg Xaa Gly Thr Ile Ile Leu

-35

-30

-25

Gly Thr Trp Tyr Met Val Val Asp Leu Leu Met Ala Yaa Lau Leu Tha

Gly Thr Trp Tyr Met Val Val Asn Leu Leu Met Ala Xaa Leu Leu Thr
-20
-15
-10

Val Glu Val Thr His Pro Asn Ser Met Pro Ala Val Asn Ile Gln Tyr

-5

5

10

Glu Val Ile Gly Asn Tyr Tyr Ser Ser Gly Asn Man Ala 2

Glu Val Ile Gly Asn Tyr Tyr Ser Ser Glu Arg Met Ala Asp Asn
15 20 25

<210> 1469

<211> 94

<212> PRT

<213> Homo sapiens

<220>

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<222> -31..-1

<400> 1469

Met Ala Ala Ala Thr Leu Thr Ser Lys Leu Tyr Ser Leu Leu Phe Arg
-30 -25 -20

Arg Thr Ser Thr Phe Ala Leu Thr Ile Xaa Arg Xaa Xaa Ser Cys Ser -15 -5 1

Ser Xaa Ala Pro Ser Ile Lys Ala Arg Thr Leu Ser Thr Thr Thr Ser 5 10 15

Thr Arg Gly Ser Cys Gly Asn Thr Ser Ser Thr Ser Met Arg Thr Ser 20 25 30

Ser Ser Leu Glu Ala Pro Ile Gln Ala Arg Arg Thr Arg Ser Thr Gln
35 40 45

Gln Leu Phe Ala Gln Ser Trp Ser Leu Ser Xaa Lys Met Met 50 55 60

<210> 1470

<211> 83

<212> PRT

<213> Homo sapiens

<220>

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<222> -41..-1

<400> 1470

Met Lys Ala Ile Lys Lys Ser Leu Thr Glu Glu Glu Tyr Leu Tyr Leu
-40 -35 -30

Asp Phe Ser His Gln Thr Glu Gly Cys Ile Phe Pro Leu His Thr Ser
-25 -20 -15 -10

Val Thr Leu Phe Leu Leu Ser Tyr Cys Asp Cys Lys Ile Phe Lys Ile
-5 1 5

Cys Leu Val Val Thr Lys Glu Val Ser Arg Asp Xaa Ser Leu Leu Arg

Asp Asp Leu Ile Gln Asp Val Glu Ile Gln Ile Ile Ser Arg Gln Glu 25 30 35

Leu Pro Pro

40

<210> 1471

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 <213> Homo sapiens
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 <400> 1471
 Met Phe Leu Cys Val Cys Tyr Phe Ile Arg Lys Ser Thr Ser Phe Phe
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 Ser Ile Ser Ser
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 <210> 1472
 <211> 71
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 <222> -45..-1
 <400> 1472
Met Gly Lys Pro Arg Gly Glu Met Leu Glu Val Val Lys Thr Val
                    -40
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Ser Thr Phe Thr Leu Gly Gly Trp Lys Gly Thr Ala Pro Val Ser Cys
                -25
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Ala Trp Trp Leu Leu Pro Val Trp Lys Leu Gly Gly Gln Leu Glu
  -10
                                - 5
Arg Arg Lys Asn Pro Lys Glu Tyr Cys Leu Gly Ser Trp Val Trp Leu
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Ser Pro Gln Leu Ala Pro Arq
<210> 1473
<211> 18
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<213> Homo sapiens
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<222> -16..-1
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Met Leu Ile Phe Thr Phe Ile Ser Thr Leu Leu Phe Val Phe Leu Gly
                        -10
Val Val
<210> 1474
<211> 47
<212> PRT
<213> Homo sapiens
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<222> -37..-1
<400> 1474
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Met Glu Val Leu Ser Xaa Pro Asn Ser Phe Gln Thr Gln Ala Leu Trp
-35
-30
-25

Asp Ser Leu His Ser Pro Gly Val Pro Gly Ser Gly Leu Cys Ser Met
-20
-15
-10

Ala Ala Val Gln Ala Gly Asn Gln Ala Ile Tyr Ser Ala Ser Gly

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. -5
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 <210> 1475
 <211> 47
 <212> PRT
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 <222> -42..-1
 <400> 1475
 Met Gln Ala Thr Ala Ser Gln Pro Ile His Phe Phe Xaa Ser Ser Pro
                             -35
 Gln Ala Pro Arg His His Ser Gly His Pro Val Pro Leu Leu Thr
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 Gln Ala Gly Phe Pro Arg Arg Gly Glu Ala Ala Pro Pro Leu Leu
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 <210> 1476
 <211> 34
 <212> PRT
 <213> Homo sapiens
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 <400> 1476
Met Arg Gly Xaa Asn Xaa Val Phe Arg Val Phe Ser Glu Ser Leu Lys
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Gly Leu Cys Thr Phe Thr Leu Asn Leu Thr Ala Val Arg Thr Ile Xaa
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Leu Asp
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<211> 40
<212> PRT
<213> Homo sapiens
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<221> SIGNAL
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<400> 1477
Met Gly Arg Ile Ile Pro Met Val Glu Lys Ala Asp Thr Ala Gln Lys
        -30
                            -25
Phe Gln Gly Arg Leu Thr Ile Ser Thr Xaa Leu Ser Thr Ser Xaa Xaa
                        -10
Phe Met Glu Leu Ser Ser Leu Arg
<210> 1478
<211> 112
<212> PRT
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<222> -67..-1
Met Asn Leu Val Ile Cys Val Leu Leu Leu Ser Ile Trp Lys Asn Asn
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 Cys Met Thr Thr Asn Gln Thr Asn Gly Ser Ser Thr Thr Gly Asp Lys
                       -45
                                            -40
 Pro Val Glu Ser Met Gln Thr Lys Leu Asn Tyr Leu Arg Arg Asn Leu
                    -30
                                        -25
Leu Ile Leu Val Gly Ile Ile Ile Met Val Phe Val Phe Ile Cys Phe
                -15
                                    -10
                                                        - 5
Cys Tyr Leu His Tyr Asn Cys Leu Ser Asp Asp Ala Ser Lys Ala Gly
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Met Val Lys Lys Gly Ile Ala Ala Lys Ser Ser Lys Thr Ser Phe
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Ser Glu Ala Lys Thr Ala Ser Gln Cys Ser Ser Glu Thr Gln Thr Gly
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<211> 35
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<213> Homo sapiens
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<400> 1479
Met Gln Ile Ser Ala Ala Ser Leu Asn Phe Ser Ser Lys Asn Gly Ile
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Phe Phe Ser Leu Thr Leu Ser Gly Cys Lys Phe Ser Lys Leu Leu Cys
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Pro Phe Gly
<210> 1480
<211> 72
<212> PRT
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Met Ile Phe Glu Pro Val Val Leu Lys Pro Val Phe Leu Asn Ile Phe
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                           -45
                                               -40
Phe Phe Ser His His Val Phe Thr Val Phe Phe Ser Gly Ser His Val
   -35
                        -30
                                            -25
Asp Ile Leu Ser Arg Thr Val Leu Val Trp Asp Cys Leu Leu Pro Pro
                   -15
                                       -10
Pro Ser Phe Phe Leu Leu Leu Ser Ser Ser Xaa Ser Xaa Leu Leu
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Leu Xaa Xaa Ser Ser Ser Ser Arg
<210> 1481
<211> 20
<212> PRT
<213> Homo sapiens
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<221> SIGNAL
<222> -14..-1
<400> 1481
Met Leu Val Pro Leu Leu Ser His Leu Leu Phe Lys Phe Thr Trp Pro
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WO 99/53051
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 Lys Xaa Ser Gln
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 <400> 1482
 Met Asp Arg Asn Pro Ser Pro Pro Pro Pro Gly Arg Asp Lys Glu Glu
                 -45
                                     -40
 Glu Glu Glu Val Ala Gly Gly Asp Cys Ile Gly Ser Thr Val Tyr Ser
                                 -25
                                                     -20
 Lys His Trp Leu Phe Gly Val Leu Ser Gly Leu Xaa Gln Xaa Val Ser
                            -10
                                                 -5
 Pro Gly Lys His Gln Asn Leu Gly Ser Xaa Xaa Glu Glu Gln Leu Thr
                                        10
 Glu Leu Asp Glu Arg Asn
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 <210> 1483
 <211> 37
 <212> PRT
 <213> Homo sapiens
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 <221> SIGNAL
 <222> -23..-1
 <400> 1483
 Met Lys Leu Ser Leu Ala Gly Tyr Glu Ile Leu Gly Cys His Phe Phe
            -20
                                -15
                                                     -10
 Ser Leu Ala Leu Leu Asn Thr Gly Pro Gln Tyr Leu Leu Ala Tyr Arg
       -5
                             1
 Val Ser Ala Glu Arg
 <210> 1484
 <211> 48
 <212> PRT
<213> Homo sapiens
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 <221> SIGNAL
 <222> -40..-1
 Met Ala Thr Ser Val Gly His Arg Cys Leu Gly Leu Leu His Gly Val
                    -35
                                 -30
 Ala Pro Trp Arg Ser Ser Leu His Pro Cys Glu Ile Thr Ala Leu Ser
                -20
                                    -15
 Gln Ser Leu Gln Pro Leu Arg Lys Leu Pro Phe Arg Ala Ser Xaa Thr
 <210> 1485
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<212> PRT

<213> Homo sapiens

<213> Homo sapiens

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Met Ala Pro Lys Gly Lys Val Gly Thr Arg Gly Lys Lys Gln Ile Phe
               -45
Glu Glu Asn Arg Glu Thr Leu Lys Phe Tyr Leu Arg Ile Ile Leu Gly
           -30
                                -25
Ala Asn Ala Ile Tyr Cys Leu Val Thr Leu Val Phe Phe Tyr Ser Ser
                            -10
Ala Ser Phe Trp Ala Trp Leu Ala Leu Gly Phe Ser Leu Ala Val Tyr
                                        10
Gly Ala Ser Tyr His Ser Met Ser Ser Met Ala Arg Ala Ala Phe Ser
                20
Glu Asp Gly Ala Leu Met Asp Gly Gly Met Asp Leu Asn Met Glu Gln
                                40
Gly Met Ala Glu His Leu Lys Asp Val Ile Leu Leu Thr Ala Ile Val
                            55
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Gln Val Leu Ser Cys Phe Ser Leu Tyr Val Trp Ser Phe Trp
<210> 1486
<211> 55
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<213> Homo sapiens
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<221> SIGNAL
<222> -29..-1
<400> 1486
Met Ala Ala Val Thr Val Thr Lys Thr Ala Ala Ala Ala Thr
               -25
                                   -20
Ala Phe Asn Lys Ala Val Trp Phe Thr Pro Cys Ser Cys Gln Glu Val
       -10
                               - 5
Ser Ser Arg Leu Pro Ala Arg Thr Ala Ala Thr Arg Gln Asp Arg Ala
                       10
Asp Lys Lys Glu Arg Pro Cys
<210> 1487
<211> 34
<212> PRT
<213> Homo sapiens
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<221> SIGNAL
<222> -19..-1
<400> 1487
Met Leu Gln Phe Glu Lys Pro Gly Ser Ala Ile Cys Leu Trp His Ser
Thr Leu Gly Gly Xaa Gly Gly Arg Glu Ile Xaa Ser Leu Arg Pro Ala
Cys Gly
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<210> 1488
<211> 24
<212> PRT
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<222> -18..-1
<400> 1488
Met Leu Ile Ser Tyr Leu Ala Ile Leu Leu Lys Trp Val Ser Asn Ser'
         -15
                              -10
Lys Ser Phe Leu Val Lys Ala Ser
   1
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<211> 76
<212> PRT
<213> Homo sapiens
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<221> SIGNAL
<222> -15..-1
<400> 1489
Met Lys Leu Gln Thr Leu Ala Phe Trp Ser Ala Tyr Val Pro Cys Gln
-15 -10 -5
Thr Gln Asp Arg Asp Ala Pro Arg Leu Thr Leu Glu Gln Ile Asp Leu
                             10
Ile Arg Arg Met Cys Ala Ser Tyr Ser Glu Leu Glu Leu Val Thr Ser
     20
                         25
Ala Lys Ala Leu Asn Asp Thr Gln Lys Leu Ala Cys Leu Ile Gly Val
                      40
Glu Gly Gly His Ser Leu Asp Asn Ser Leu Ser Arg
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<210> 1490
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<221> SIGNAL
<222> -14..-1
<400> 1490
Met Pro Ala Cys Leu Ser Ser Phe Val Ile Pro Ser Leu Leu Ser Pro
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Ser Ser Pro Pro Ser Ile Gly
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<210> 1491
<211> 34
<212> PRT
<213> Homo sapiens
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<222> -16..-1
<400> 1491
Met Val Val Ser Phe Ala Gly Ser Cys Thr Ile Leu Gly Ala Ser Ser
               -10
His Ser Phe Pro Ile Glu Val Ser Leu Phe Pro Val Asp Cys Gly Phe
1
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Leu Leu
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637
<210> 1492
<211> 32
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<213> Homo sapiens
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<222> -20..-1
<400> 1492
Met Cys Cys Pro Gly Trp Asn Ala Val Ser Gln Ser Trp Leu Ala Ala
                   -15
                                        -10
Pro Ser Thr Ser Trp Val Gln Glu Ile Leu Val Leu Gln Pro Pro Gly
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<210> 1493
<211> 69
<212> PRT
<213> Homo sapiens
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<221> SIGNAL
<222> -54..-1
<400> 1493
Met Gly Glu Ile Lys Val Ser Pro Asp Tyr Asn Trp Phe Arg Gly Thr
               -50
                     -45
Val Pro Leu Lys Xaa Xaa Xaa Val Asp Asp Asp Ser Lys Ile Trp
           -35
                               -30
Ser Xaa Tyr Asp Ala Gly Pro Arg Ser Ile Arg Cys Pro Leu Ile Phe
                       -15
       -20
                                               -10
Leu Xaa Xaa Val Ser Gly Thr Xaa Asp Val Phe Phe Arg Gln Ile Leu
  - 5
Ala Leu Thr Gly Trp
<210> 1494
<211> 45
<212> PRT
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<222> -16..-1
<400> 1494
Met Asp Ala Ser His Ser His Leu Ser Leu Val Gly His Ser Arg Ala
                       -10
Cys Gly Val Thr Ser Arg Pro His Ala Arg His Arg Gly Arg Cys Leu
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Gly Pro Cys Ser Arg Ser Gly Pro Arg Leu Cys Ser Ala
<210> 1495
<211> 61
<212> PRT
<213> Homo sapiens
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<400> 1495

638 Met Gly Ser Asn Ala Val Val Trp His Thr Lys Pro Ser Leu Leu Asn -30 -25 His Pro Ala Ser Ser Leu Ile Ser His Asp Pro Trp Pro Arg Gly Ala -15 -10 Phe Ala Leu Ser Cys Pro Ser Ala Ser Phe Met Leu Phe Ser Ser Leu 10 Gln Cys Pro Phe Pro Tyr Xaa Xaa Thr Glu Cys Asn Xaa <210> 1496 <211> 56 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -18..-1 <400> 1496 Met Lys Glu Asp Gly Ala Cys Leu Phe Arg Ala Val Ala Asp Gln Val -15 -10 -5 Tyr Gly Asp Gln Asp Met His Glu Val Val Arg Lys His Xaa Met Asp 10 Tyr Leu Met Lys Asn Ala Asp Tyr Phe Ser Xaa Tyr Val Thr Glu Asp 20 15 25 Phe Thr Thr Tyr Ile Xaa Arg Lys 35 <210> 1497 <211> 24 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -21..-1 <400> 1497 Met Val His Leu Ile Leu Thr Glu Val Leu Ile Met Ile Xaa Glu Ala -15 Xaa Asn Val Trp Cys Gly Asp Ser -5 <210> 1498 <211> 51 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -47...-1 <400> 1498 Met Tyr His Asn Leu Phe Ala Leu Leu Leu Ile Asp Ile His Val Val -40 -45 Leu Val Phe Tyr Cys Leu Asp Leu Leu Met Ile His Ile Phe Tyr Cys -25 -20 Lys Tyr Cys Leu Xaa Phe Gly Ile Leu Ala Ser Glu Val Tyr Ser Trp -10 -5 -15 Asn Ile Tyr <210> 1499

<211> 44

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<213> Homo sapiens
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<222> -29..-1
<400> 1499
Met Glu Ser Pro Ser Arg Ala Gly Gly Val Xaa Leu Xaa Lys Ala Ala
               -25
                                    -20
Ser Pro Leu Cys Ser Xaa Ser Ser Gly Tyr Cys Xaa Ala Phe Pro Arg
    -10
                               -5
Arg Ser Ala Arg Arg His Leu His Pro Gly His Gly
                       10
<210> 1500
<211> 61
<212> PRT
<213> Homo sapiens
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<221> SIGNAL
<222> -25..-1
<400> 1500
Met Trp Arg Tyr Val Ser Arg Leu Ser Ser Val Pro Leu Ile Ser Leu
                   -20
                                      -15
Ser Val Leu Met Pro Val Gln His Ser Pro Asp Phe Cys Ser Phe Ile
               - 5
                                   1
Val Ser Thr Val Ile Pro Trp Phe Pro Trp Gly Ile Gly Ser Arg Thr
                           15
Leu Met Asp Ile Lys Ile Leu Gly Cys Ser Ser Pro Gly
                       30
<210> 1501
<211> 33
<212> PRT
<213> Homo sapiens
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<221> SIGNAL
<222> -30..-1
<400> 1501
Met Asp Val Ser Cys Lys Ile Leu Tyr Asn Val Ile Glu Lys Phe Cys
                -25
                           -20
Asn Asn Leu Leu Lys Leu Ser Ser His Ser Pro Thr Cys Ala Cys Lys
               -10
                                   - 5
Leu
<210> 1502
<211> 29
<212> PRT
<213> Homo sapiens
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<221> SIGNAL
<222> -20..-1
<400> 1502
Met Ile Phe Lys Asp Val Phe Ser His Leu Ser Gly Ser Ser Leu Gln
                   -15
                                       -10
Leu Cys Val Ala Gln Phe Leu Xaa Leu Ser Ala Val Asp
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<211> 115 <212> PRT

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<210> 1503
<211> 50
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -44..-1
<400> 1503
Met. Lys Leu Thr Lys Asn Ile Leu Xaa Val Ile Ile Gly Cys Phe Lys
            -40
                           -35
Leu Ile Ala Tyr Lys Asn Ser Val Leu Tyr Phe Tyr Ser Asn Phe Ser
           -25
                               -20
Phe Ser Phe Leu Phe Phe Phe Leu Ser Phe Phe Phe Phe Phe Phe
Phe Phe
<210> 1504
<211> 92
<212> PRT
<213> Homo sapiens
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<221> SIGNAL
<222> -87..-1
<400> 1504
Met Asn Asn Gln Lys Gln Xaa Xaa Pro Thr Leu Ser Gly Gln Arg Phe
                           -80
                                              -75
Lys Thr Arg Lys Arg Asp Glu Lys Glu Arg Phe Asp Pro Thr Gln Phe
                       -65
                                           -60
Gln Asp Cys Ile Ile Gln Gly Leu Thr Glu Thr Gly Thr Asp Leu Glu
                   -50
                                       -45
Ala Val Ala Lys Phe Leu Asp Ala Ser Gly Ala Lys Leu Asp Tyr Arg.
               -35
                                   -30
Arg Tyr Ala Glu Thr Leu Phe Asp Ile Leu Val Ala Gly Xaa Met Leu
           -20
                               -15
Ala Pro Gly Gly Thr Leu Ala Asp Asp Met Met Xaa
<210> 1505
<211> 35
<212> PRT
<213> Homo sapiens
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<221> SIGNAL
<222> -17..-1
<400> 1505
Met Ala Asp Ser Leu Glu Ile Lys Leu Pro Phe Leu Pro Phe Ala Gln
      -15
                           -10
                                               -5
Gln Ile Asp Ile Lys Ser Cys Phe Tyr Phe Phe Yaa Asn Xaa Xaa
                                       10
  1
Phe Pro Arg
<210> 1506
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641

<221> SIGNAL <222> -35..-1

<400> 1506

Met Asp Arg Lys Trp Thr Trp Lys Arg Gly Gln Arg Ser His Leu Glu
-35 -30 -25 -20

Ser Gly Gln Ala Ala Pro Ala Thr Ala Ala Ala Thr Ala Ala Ser Ala
-15
-10
-5

Thr Thr Gly Ala Ser Val Trp Arg Ser Thr Met Gly Xaa Leu Cys Asp

Cys Thr Xaa Xaa Pro Tyr Glu Gly Pro Phe Cys Lys Lys Glu Val Ser 15 20 25

Ala Val Phe Glu Ala Gly Thr Ser Val Thr Tyr Met Phe Gln Glu Pro 30 40 45

Tyr Pro Val Thr Lys Asn Ile Ser Leu Ser Ser Ser Ala Ile Tyr Thr
50 55 60

Asp Ser Ala Pro Ser Lys Glu Asn Ile Ala Leu Ser Phe Val Thr Thr
65 70 75

Gln Ala Pro 80

<210> 1507

<211> 74

<212> PRT

<213> Homo sapiens

<220>

<221> SIGNAL

<222> -43..-1

<400> 1507

Met Ala Pro Gln Met Tyr Glu Phe His Leu Pro Leu Ser Pro Glu Glu
-40 -35 -30

Leu Leu Lys Ser Gly Gly Val Asn Gln Tyr Val Val Gln Glu Val Leu
-25
-20
-15

Ser Ile Lys His Leu Pro Pro Gln Leu Arg Ala Phe Gln Ala Ala Phe
-10 -5 1 5

Arg Ala Gln Gly Pro Leu Ala Met Leu Gln His Phe Asp Thr Ile Tyr 10 15 20

Ser Ile Leu His His Phe Arg Ser Ile Asp

<210> 1508

<211> 84

<212> PRT

<213> Homo sapiens

<220>

<221> SIGNAL

<222> -15..-1

<400× 1508

Met Ala Ala Val Gln Val Gly Ser Trp Pro Ser Val Gln Pro Arg

Glu Ala Pro Arg Glu Ala Ile Pro Glu Arg Gly Asn Gly Phe Arg Leu
5 10 15

Leu Ser Ala Arg Leu Cys Ala Leu Arg Pro Asp Asp Ser Ser Ser Ala 20 25 30

Arg Thr Glu Ile His Leu Xaa Phe Asp Gln Leu Ile Ser Glu Asn Tyr

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Ser Glu Gly Ser Gly Val Ala Pro Glu Asp Val Ser Ala Leu Leu Val
                     55
Gln Ala Cys Gly
 <210> 1509
 <211> 48
 <212> PRT
 <213> Homo sapiens
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 <222> -30..-1
 <400> 1509
Met Phe His Gly Cys His Ile Leu Ser Phe Leu Arg Ile Ser Thr Arg
                    -25
                                         -20
-30
Gly Phe Leu Phe Phe Leu Gln Phe Ser Phe Pro Leu Tyr Tyr Leu Phe
                -10
Arg Xaa Xaa Phe Pro Gln Ser Phe Met Leu Glu Ala Phe Val Arg Cys
      5
                             10
<210> 1510
<211> 42
<212> PRT
<213> Homo sapiens
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<221> SIGNAL
<222> -26..-1
<400> 1510
Met Tyr Arg His Ser Lys Gln Arg Asn Asn Val Pro Cys Leu Val Leu
  -25
                        -20
                                             -15
Tyr Ala Pro Trp Val Pro Pro Leu Leu Leu Ala Phe Trp Gly Trp Trp
-10
                    -5
Leu Leu Glu Gln Gly Leu Phe Phe Phe
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<210> 1511
<211> 137
<212> PRT
<213> Homo sapiens
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<221> SIGNAL
<222> -50..-1
<400> 1511
Met Gly Asp Pro Ser Lys Gln Asp Ile Leu Thr Ile Phe Lys Arg Leu
                   -45
Arg Ser Val Pro Thr Asn Lys Val Cys Phe Asp Cys Gly Ala Lys Asn
                                    -25
Pro Ser Trp Ala Ser Ile Thr Tyr Gly Val Phe Leu Cys Ile Asp Cys
                                -10
Ser Gly Ser His Arg Ser Leu Gly Val His Leu Ser Phe Ile Arg Ser
Thr Glu Leu Asp Ser Asn Trp Ser Trp Phe Gln Leu Arg Cys Met Gln
                    20
Val Gly Gly Asn Ala Ser Ala Ser Ser Phe Phe His Gln His Gly Cys
                35
                                    40
                                                        45
Ser Thr Asn Asp Thr Asn Ala Lys Tyr Asn Ser Arg Ala Ala Gln Leu
Tyr Arg Glu Lys Ile Lys Ser Leu Ala Ser Gln Ala Thr Arg Lys His
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65
                           70
                                               75
Gly Thr Asp Leu Trp Leu Asp Ser Cys
    80
                   85
<210> 1512
<211> 26
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<213> Homo sapiens
<220>
<221> SIGNAL
<222> -22..-1
<400> 1512
Met Pro Leu Pro Pro Asn Gln Ser Pro Leu Leu His Leu Val Phe
    -20
                           -15
His Gln Arg Thr Leu Ile Ser Leu Pro Pro
<210> 1513
<211> 21
<212> PRT
<213> Homo sapiens
<221> SIGNAL
<222> -13..-1
<400> 1513
Met Phe Leu Thr Phe Phe Cys Thr Gln Val His Gly Pro Ser Ile
           -10
Leu Asp Ser Pro Ala
  5
<210> 1514
<211> 56
<212> PRT
<213> Homo sapiens
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<221> SIGNAL
<222> -14..-1
<400> 1514
Met Val Thr Leu Trp Ile Phe Gln Phe Phe Leu Cys Leu Thr Cys Lys
                    -5
               -10
Ala Tyr Asn Leu Arg Asn Cys Asn Asp Gly Lys Gly Xaa Xaa Ser Xaa
                           10
Val Leu Gly Leu Glu Gln Xaa Leu Pro Glu Ser Ala Gly Met Val Xaa
Phe Leu Gly Leu Lys His Arg Trp
35
<210> 1515
<211> 37
<212> PRT
<213> Homo sapiens
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<222> -14..-1
<400> 1515
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Met Val Leu Trp Ala Gly Pro Xaa Val Pro Leu Leu Cys Ala Ala Xaa
Gly Leu Gly Ala Leu His Pro Arg Cys Ser Ser Gln Gly Leu Arg Leu
                             10
Ala Xaa Ser Glu Ala
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<210> 1516
<211> 61
<212> PRT
<213> Homo sapiens
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<221> SIGNAL
<222> -41..-1
<400> 1516
Met Asn Trp Arg Arg Lys Ser Val Ile Gly Leu Ser Phe Asp Phe Val
                        -35
Ala Leu Asn Leu Thr Gly Phe Val Ala Tyr Ser Val Phe Asn Ile Gly
                    -20
                                        -15
Leu Leu Trp Val Pro Xaa Xaa Xaa Gly Ala Val Ser Pro Gln Ile Pro
                -5
Gln Arg Ser Glu Pro Arg Glu Gln Gln Arg Arg Leu Leu
<210> 1517
<211> 149
<212> PRT
<213> Homo sapiens
<400> 1517
Met Glu Pro Leu Ala Ala Tyr Pro Leu Lys Cys Ser Gly Pro Arg Ala
                                    10
Lys Val Phe Ala Val Leu Leu Ser Ile Val Leu Cys Thr Val Thr Leu
Phe Leu Leu Gln Leu Lys Xaa Leu Lys Pro Lys Ile Asn Ser Phe Tyr
Ala Phe Glu Val Lys Asp Ala Lys Gly Arg Thr Val Ser Leu Glu Lys
                        55
Tyr Lys Gly Lys Val Ser Leu Val Val Asn Val Ala Ser Asp Cys Gln
                    70
Leu Thr Asp Arg Asn Tyr Leu Gly Leu Lys Glu Leu His Lys Glu Phe
Gly Pro Ser His Phe Ser Val Leu Ala Phe Pro Cys Asn Gln Phe Gly
            100
                                105
Glu Ser Glu Pro Arg Pro Ser Lys Glu Val Glu Ser Phe Ala Arg Lys
                            120
                                                125
Asn Tyr Gly Val Thr Phe Pro Ile Phe His Lys Ile Lys Ile Leu Gly
                        135
Ser Glu Gly Glu Leu
145
<210> 1518
<211> 132
<212> PRT
<213> Homo sapiens
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Met Asn Glu Ala Met Ala Thr Asp Ser Pro Arg Arg Pro Ser Arg Cys
Thr Gly Gly Val Val Arg Pro Gln Ala Val Thr Glu Gln Ser Tyr
                                25
Met Glu Ser Val Val Thr Phe Leu Gln Asp Val Val Pro Gln Ala Tyr
                            40
```

Ser Gly Thr Pro Leu Thr Glu Glu Lys Glu Lys Ile Val Trp Val Arg 55 Phe Glu Asn Ala Asp Leu Asn Asp Thr Ser Arg Asn Leu Glu Phe His Glu Ile His Ser Thr Gly Ser Glu Pro Pro Leu Leu Ile Met Ile Gly 85 Tyr Ser Asp Gly Met Gln Val Trp Ser Ile Pro Ile Xaa Gly Glu Xaa 105 . 110 Lys Ser Ser Ser Leu Phe Asp Met Ala Gln Phe Glu Arg Leu Glu Ser 115 120 Cys Leu Leu His 130 <210> 1519 <211> 46 <212> PRT <213> Homo sapiens <400> 1519 Met Pro Val Thr Arg Ala Ser Gln Pro Arg Lys Pro Ser Ser Ala Gln 10 Gln Gln Lys Ala Ala Leu Leu Xaa Asn Asn Thr Ala Leu Gln Ser Val 20 25 Ser Leu Arg Ser Lys Thr Thr Ile Arg Glu Arg Pro Ser Ser 40 <210> 1520 <211> 41 <212> PRT <213> Homo sapiens <400> 1520 Met Asn Gly Phe Gly Arg Leu Glu His Phe Ser Gly Ala Val Tyr Glu 10 Gly Gln Phe Lys Asp Asn Met Phe His Gly Leu Gly Thr Tyr Thr Phe 20 25 Pro Asn Gly Ala Lys Tyr Thr Gly Ile 35 <210> 1521 <211> 131 <212> PRT <213> Homo sapiens <400> 1521 Met Ala Lys Ile Ala Lys Thr His Glu Asp Ile Glu Ala Gln Ile Arg Glu Ile Gln Gly Lys Lys Ala Ala Leu Asp Glu Ala Gln Gly Val Gly Leu Asp Ser Thr Gly Tyr Tyr Asp Gln Glu Ile Tyr Gly Gly Ser Asp Ser Arg Phe Ala Gly Tyr Val Thr Ser Ile Ala Ala Thr Glu Leu Glu 55 Asp Asp Asp Asp Tyr Ser Ser Ser Thr Ser Leu Leu Gly Gln Lys 70 75 Lys Pro Gly Tyr His Ala Pro Val Ala Leu Leu Asn Asp Ile Pro Gln Ser Thr Glu Gln Tyr Asp Pro Phe Ala Glu His Arg Pro Pro Lys Ile 105 110 Ala Asp Arg Glu Asp Glu Tyr Lys Lys His Arg Arg Thr Met Ile Ile 120 Ser Gln Ser 130 <210> 1522

<211> 82

PCT/IB99/00712

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<212> PRT
<213> Homo sapiens
<400> 1522
Met Pro Ile Asn Ly
1 5
Val Val Val Arg Cy
20
Tyr Lys Gln Ala Va
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Met Pro Ile Asn Lys Ser Glu Lys Pro Glu Ser Cys Asp Asn Val Lys

1 5 10 15

Val Val Val Arg Cys Arg Pro Leu Asn Glu Arg Glu Lys Ser Met Cys
20 25 30

646

Tyr Lys Gln Ala Val Ser Val Asp Glu Met Arg Gly Thr Ile Thr Val 35 40 45

His Lys Thr Asp Ser Ser Asn Glu Pro Pro Lys Thr Phe Thr Phe Asp 50 55 60

Thr Val Phe Gly Pro Glu Ser Lys Gln Leu Asp Val Tyr Asn Leu Thr 65 70 75 80

Ala Arg

<210> 1523 <211> 40 <212> PRT

<213> Homo sapiens

<400> 1523

 Met
 Pro
 Asn
 Arg
 Gly
 Asn
 Gly
 Leu
 Ala
 Pro
 Gly
 Asp
 Arg
 Phe

 1
 5
 5
 10
 15
 15

 Lys
 Pro
 Val
 Pro
 Pro
 His
 Val
 Glu
 Gly
 Val
 Glu
 Val
 Asp
 Leu

 20
 25
 30

Glu Ser Ile Arg Arg Ile Asn Lys 35 40

<210> 1524 <211> 35

<212> PRT <213> Homo sapiens

<400> 1524

Met Ser Leu Trp Leu Cys Phe Gln Cys Pro Leu Gly Val Ser Lys Ser 1 5 10 15

Asn Lys Lys Arg Ile Asn Leu Cys Asn Gly Phe Trp Asn Glu Lys Ile

Lys Asn Arg

<210> 1525

<211> 47

<212> PRT

<213> Homo sapiens

<400> 1525

Met Gly Thr His Val Phe Ala Ile Asn Lys Arg Thr Tyr Val Ile Ser

1 10 15

Arg Asp Arg Glu Leu Ser Thr Ala Lys Pro Xaa Cys Ser Ser Leu Leu 20 25 30

Thr Ala Pro Val Leu Cys Tyr Trp Arg Ala Cys Pro Leu Gln Thr 35 40 45

<210> 1526

<211> 56

<212> PRT

<213> Homo sapiens

<400> 1526

Met Phe Cys Phe Leu Phe Ser Trp Trp Leu Arg Gly Gly Leu His Val

Leu Leu Asn Thr Cys Leu Tyr Val Pro Tyr Gly Tyr Leu Ser Leu Ile 20 25 30

Cys Leu Cys Leu Trp Tyr Leu Asn Leu Tyr Lys Phe Ser Ile Phe
35 40

Phe Ser Phe Leu Ser Phe Phe

50

<210> 1527

<211> 55 <212> PRT

<213> Homo sapiens

<400> 1527

Met Thr Thr Thr Ser Lys His Ala Ala Tyr Cys Leu Lys Gly Ser Cys 1 5 10 15

.55

Leu Xaa Gln Ala Arg Val Gln Trp Pro Leu Lys Xaa Thr Thr Ala Ser 20 25 30

Asn Phe Trp Ala Gln Val Ile Leu Ser Leu Pro Val Val Phe Val Asp 35 40 . 45

Cys Leu Met Glu Xaa His Gly 50 55

<210> 1528

<211> 121

<212> PRT

<213> Homo sapiens

<400> 1528

Met Glu Gly Gly Gly Ile Pro Leu Glu Thr Leu Lys Glu Glu Ser

1 10 15

Gln Ser Arg His Val Leu Pro Ala Ser Phe Glu Val Asn Ser Leu Gln
20 25 30

Lys Ser Asn Trp Gly Phe Leu Leu Thr Gly Leu Val Gly Gly Thr Leu
35 40 45

Val Ala Val Tyr Ala Val Ala Thr Pro Phe Val Thr Pro Ala Leu Arg
50 55 60

Lys Val Cys Leu Pro Phe Val Pro Ala Thr Met Lys Gln Ile Glu Asn 65 70 75 80

Val Val Lys Met Leu Arg Cys Arg Arg Gly Ser Leu Val Asp Ile Gly 85 90 95

Ser Gly Asp Gly Arg Ile Val Ile Ala Ala Ala Lys Lys Gly Phe Xaa 100 105 110

Ala Val Gly Tyr Glu Leu Asn Pro Trp 115 120

<210> 1529

<211> 154

<212> PRT

<213> Homo sapiens

<400> 1529

Met Ala Thr Pro Leu Ala Val Asn Ser Ala Ala Ser Leu Trp Gly Pro 1 5 10 15

Tyr Lys Asp Ile Trp His Lys Val Gly Asn Ala Leu Trp Arg Gln
20 25 30

Pro Glu Ala Val Xaa Leu Leu Asp Lys Ile Leu Lys Lys His Lys Pro 35 40 45

Asp Phe Ile Ser Leu Phe Lys Asn Pro Pro Lys Asn Val Gln Gln His
50 55 60

Glu Lys Val Gln Lys Ala Ser Thr Glu Gly Val Ala Ile Gln Gly Gln

Gln Gly Thr Arg Leu Leu Pro Glu Gln Leu Ile Lys Glu Ala Phe Ile

Leu Ser Asp Leu Phe Asp Ile Gly Glu Leu Ala Ala Val Glu Leu Leu
100 105 110

Leu Ala Gly Glu His Gln Gln Pro His Phe Pro Gly Leu Thr Arg Gly
115 120 125

Leu Val Ala Val Leu Leu Tyr Trp Asp Gly Lys Arg Cys Ile Ala Asn 130 135 140

Ser Leu Lys Ala Leu Ile Gln Ser Arg Arg 145 150

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<210> 1530
 <211> 125
 <212> PRT
 <213> Homo sapiens
 <400> 1530
Met Asn Gly Arg Ala Asp Phe Arg Glu Pro Asn Ala Glu Val Pro Arg
                                     10
Pro Ile Pro His Ile Gly Pro Asp Tyr Ile Pro Thr Glu Glu Glu Arg
                                 25
Arg Val Phe Ala Glu Cys Asn Asp Glu Ser Phe Trp Phe Arg Ser Val
Pro Leu Ala Ala Thr Ser Met Leu Ile Thr Gln Gly Leu Ile Ser Lys
                         55
                                             60
Gly Ile Leu Ser Ser His Pro Lys Tyr Gly Ser Ile Pro Lys Leu Ile
65
                    70
                                         75
Leu Ala Cys Ile Met Gly Tyr Phe Ala Gly Lys Leu Ser Tyr Val Lys
                                     90
Thr Cys Gln Glu Lys Phe Lys Lys Leu Glu Asn Ser Pro Leu Gly Glu
            100
                                 105
Ala Leu Arg Ser Gly Gln Ala Arg Arg Ser Ser Pro Pro
<210> 1531
<211> 35
<212> PRT
<213> Homo sapiens
<400> 1531
Met His Met Ser Lys Leu Ile Asn Leu Tyr Thr Ser Xaa Met Cys Asn
1
                                     10
Leu Leu Xaa Ile His Leu Xaa Xaa Ile Ser Cys Leu Xaa Asn Asn Lys
Xaa Thr Leu
        35
<210> 1532
<211> 111
<212> PRT
<213> Homo sapiens
<400> 1532
Met Tyr Gly Lys Gly Lys Ser Asn Ser Ser Ala Val Pro Ser Asp Ser
                                    10
Gln Ala Arg Glu Lys Leu Ala Leu Tyr Val Tyr Glu Tyr Leu Leu His
                                25
Val Gly Ala Gln Lys Ser Ala Gln Thr Phe Leu Ser Glu Ile Arg Trp
                            40 .
Glu Lys Asn Ile Thr Leu Gly Glu Pro Pro Gly Phe Leu His Ser Trp
                        55
Trp Cys Val Phe Trp Asp Leu Tyr Cys Ala Ala Pro Glu Arg Arg Glu
                    70
Thr Cys Glu His Ser Ser Glu Ala Lys Ala Phe His Asp Tyr Ser Ala
                                    90
Ala Ala Ala Pro Ser Pro Val Leu Gly Asn Ile Pro Pro Gly Asp
                                105
<210> 1533
<211> 107
<212> PRT
<213> Homo sapiens
<400> 1533
Met Asn Pro Glu Tyr Asp Tyr Leu Phe Lys Leu Leu Leu Ile Gly Asp
Ser Gly Val Gly Lys Ser Cys Leu Leu Leu Arg Phe Ala Asp Asp Thr
```

30 Tyr Thr Glu Ser Tyr Ile Ser Thr Ile Gly Val Asp Phe Lys Ile Arg 40

Thr Ile Glu Leu Asp Gly Lys Thr Ile Lys Leu Gln Ile Trp Asp Thr 55

Ala Gly Gln Glu Arg Phe Arg Thr Ile Thr Ser Ser Tyr Tyr Arg Gly 75

Ala His Gly Ile Ile Val Val Tyr Asp Val Thr Asp Gln Glu Ser Tyr 85 90

Ala Xaa Val Lys Gln Trp Leu Gln Glu Ile Asp

<210> 1534

<211> 31

<212> PRT

<213> Homo sapiens

<400> 1534

Met Asn Ser Lys Ala Xaa Lys Ser Ser Thr Ala Asn Gln Gly Asp Gly 10

Asp Glu Glu Xaa Val Gly Arg Xaa Glu Xaa Ser Val Gly Glu Phe 20 25

<210> 1535

<211> 48

<212> PRT

<213> Homo sapiens

<400> 1535

Met Leu Tyr Ser Thr Leu Lys His Thr Leu Gln Tyr Val Ile Ile Asn 10

Cys Gly His His Ala Val Gln Lys Ile Ser Lys Thr Tyr Ser Ser Cys 20 25

Leu Thr Glu Xaa Leu Tyr Pro Leu Pro Asn Ile Ser Pro Ile Pro Pro

<210> 1536

<211> 94

<212> PRT

<213> Homo sapiens

<400> 1536

Met Asn Asp Glu Val Asn Pro Arg Arg Val Leu Glu Leu Met Gly Ser 10

Glu Val Thr Gln Ile Ala Cys Gly Arg Gln His Thr Leu Xaa Phe Val

Pro Ser Ser Gly Leu Ile Tyr Ala Phe Gly Cys Gly Ala Arg Gly Gln

Leu Gly Thr Gly His Thr Cys Asn Val Lys Cys Pro Ser Pro Val Lys 55

Gly Tyr Trp Ala Ala His Ser Gly Gln Leu Ser Ala Arg Ala Asp Arg

Phe Lys Tyr His Ile Val Lys Gin Ile Phe Ser Gly Gly Asp

<210> 1537

<211> 22

<212> PRT

<213> Homo sapiens

<400> 1537

Met Pro Val Arg Thr Ile Thr Arg Gln Asn Gly Ser Val Pro Trp Gly 10

Pro Asn His Cys Asp Lys

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<211> 94
 <212> PRT
 <213> Homo sapiens
 <400> 1538
 Met Gly Asp Asn Pro Phe Gln Pro Lys Ser Asn Ser Lys Met Ala Glu
                                     10
 Leu Phe Met Glu Cys Glu Glu Glu Leu Glu Pro Trp Gln Lys Lys
                                 25
 Val Lys Glu Val Glu Asp Asp Asp Asp Glu Pro Ile Phe Val Gly
                             40
 Glu Ile Ser Ser Ser Lys Pro Ala Ile Ser Asn Ile Leu Asn Arg Val
                         55
 Asn Pro Ser Ser Tyr Ser Arg Gly Leu Lys Asn Gly Ala Leu Ser Arg
                     70
 Gly Ile Thr Ala Ala Phe Lys Pro Thr Ser Gln His Tyr Thr
 <210> 1539
 <211> 67
 <212> PRT
 <213> Homo sapiens
 <400> 1539
Met Val Thr Gln Ala Gln Gln Glu Ile Thr Val Gln Gln Leu Met Ala
 1
                                     10
His Leu Asp Ala Ile Arg Lys Asp Met Val Ile Leu Glu Lys Ser Glu
             20
                              · 25
Phe Ala Asn Leu Arg Ala Glu Asn Glu Lys Met Lys Ile Glu Leu Asp
Gln Val Lys Gln Gln Leu Met His Glu Thr Ser Xaa Ile Arg Ala Asp
    50
                         55
Asn Lys Leu
65
<210> 1540
<211> 38
<212> PRT
<213> Homo sapiens
<400> 1540
Met Lys Phe Gly Asn Val Arg Met Xaa Ser Ile Gln Ile Phe Ile Val
                                    10
Ser Ile Trp Ser Phe Phe Leu Phe Tyr Gly Lys Tyr Thr Tyr Ile Arg
            20
                                25
Leu Ile Leu Ser Gln Gly
        35
<210> 1541
<211> 35
<212> PRT
<213> Homo sapiens
<400> 1541
Met Thr Phe Asp Leu Ser Val Phe Ser Thr Leu Ser Asp His Phe Tyr
                                    10
Ser Ser Ser Leu Ser Asn Thr Ala Arg Asn Leu Tyr Ile Cys Leu Phe
                                25
His Ile Thr
        35
<210> 1542
<211> 28
<212> PRT .
<213> Homo sapiens
<400> 1542
Met Gly Arg Trp Ala Leu Asp Val Ala Phe Leu Trp Lys Ala Val Leu
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651 10 Thr Leu Gly Leu Val Leu Leu Tyr Tyr Cys Phe Ser 20 <210> 1543 <211> 128 <212> PRT <213> Homo sapiens <400> 1543 Met Ala Leu His Val Pro Lys Ala Pro Gly Phe Ala Gln Met Leu Lys Glu Gly Ala Lys His Phe Ser Gly Leu Glu Glu Ala Val Tyr Arg Asn 20 Ile Gln Ala Cys Lys Glu Leu Ala Gln Thr Thr Arg Thr Ala Tyr Gly Pro Asn Gly Met Asn Lys Met Val Ile Asn His Leu Glu Lys Leu Phe Val Thr Asn Asp Ala Ala Thr Ile Leu Arg Glu Leu Glu Val Gln His 70 75 Pro Ala Ala Lys Met Ile Val Met Ala Ser His Met Gln Glu Gln Glu 90 Val Gly Asp Gly Thr Asn Phe Val Leu Val Phe Ala Gly Ala Leu Leu 100 105 Glu Leu Ala Glu Glu Leu Leu Arg Ile Gly Leu Ser Val Ser Glu Val 120 <210> 1544 <211> 33 <212> PRT <213> Homo sapiens <400> 1544 Met Ala Asn Arg Tyr Thr Met Asp Leu Thr Ala Ile Tyr Glu Ser Leu 5 10 Leu Ser Leu Ser Pro Asp Val Thr Leu Thr His Phe Ala His Cys Asn 20 25 Leu <210> 1545 <211> 68 <212> PRT <213> Homo sapiens <400> 1545 Met Met Glu Glu Ser Gly Ile Glu Thr Thr Pro Pro Gly Thr Pro Pro 10 Pro Asn Pro Ala Gly Leu Ala Ala Thr Ala Met Ser Ser Thr Pro Val 25 Pro Leu Ala Ala Thr Ser Ser Phe Ser Ser Pro Asn Val Ser Ser Met 40 Glu Ser Phe Pro Pro Leu Ala Tyr Ser Thr Pro Gln Pro Pro Leu Pro 55 Pro Val Arg Pro 65 <210> 1546 <211> 50 <212> PRT <213> Homo sapiens <400> 1546 Met Leu Cys Leu Thr Glu Gly Ala Lys Asp Glu Cys Asn Val Val Glu 10 Val Val Ala Arg Asn His Asp His Gln Glu Ile Ala Val Pro Val Ala 20 . 25 Xaa Leu Lys Leu Ser Cys Gln Pro Met Leu Ser Leu Asp Asp Phe Gln

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35
                             40
                                                  45
 Leu Gln
     50
 <210> 1547
 <211> 139
 <212> PRT
 <213> Homo sapiens
 <400> 1547
 Met Pro Thr Val Ser Val Lys Arg Asp Leu Leu Phe Gln Ala Leu Gly
                                     10
 Arg Thr Tyr Thr Asp Glu Glu Phe Asp Glu Leu Cys Phe Glu Phe Gly
 Leu Glu Leu Asp Glu Ile Thr Ser Glu Lys Glu Ile Ile Ser Lys Glu
 Gln Gly Asn Val Lys Ala Ala Gly Ala Ser Asp Val Val Leu Tyr Lys
 Ile Asp Val Pro Ala Asn Arg Tyr Asp Leu Leu Cys Leu Glu Gly Leu
 Val Arg Gly Leu Gln Val Phe Lys Glu Arg Ile Lys Ala Pro Val Tyr
                                                         95 . .
 Lys Arg Val Met Pro Asp Gly Lys Ile Gln Lys Leu Ile Ile Thr Glu
                                 105
                                                     110
 Glu Thr Ala Lys Ile Arg Pro Phe Ala Val Ala Ala Val Leu Arg Asn
                             120
 Ile Lys Phe Thr Lys Asp Arg Tyr Asp Ser Phe
     130
                         135
 <210> 1548
 <211> 71
 <212> PRT
 <213> Homo sapiens
 <400> 1548
Met Phe Ser Glu Glu Leu Trp Leu Glu Asn Glu Lys Lys Cys Ala Val
Val Arg Lys Ser Lys Gln Gly Arg Lys Arg Gln Glu Leu Leu Ala Val
Ala Phe Gly Val Lys Val His Thr Phe Arg Gly Pro His Trp Cys Glu
                             40
Tyr Cys Ala Asn Phe Met Trp Gly Leu Ile Ala Gln Gly Val Arg Cys
   50
                         55
Ser Asp Cys Gly Leu Asn Val
<210> 1549
<211> 29
<212> PRT
<213> Homo sapiens
<400> 1549
Met Val Val Phe Met Thr Tyr Val Thr Leu Pro Phe Phe Phe Ser Phe
                5
                                    10
Ile Ser Ser Leu Leu Ser Phe Phe Phe Leu Phe Leu Leu
            20
<210> 1550
<211> 50
<212> PRT
<213> Homo sapiens
Met Gln Glu Leu Phe Leu Lys Phe Val Asp Glu Asn Trp Glu Gly Ser
                                    10
Leu Lys Ser Lys Tyr Val Arg Gly Ser Asp Pro Val Leu Lys Leu Leu
            20
                                                     30
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WO 99/53051 653 Asp Asp Asn Gly Asn Ile Ala Glu Glu Leu Ser Ile Leu Lys Trp Thr 40 Gln Thr 50 <210> 1551 <211> 68 <212> PRT <213> Homo sapiens <400> 1551 Met Pro Lys Thr Met His Phe Leu Phe Arg Phe Ile Val Phe Phe Tyr Leu Trp Gly Leu Phe Thr Ala Gln Arg Gln Lys Lys Glu Glu Ser Thr Glu Glu Val Lys Ile Glu Val Leu His Arg Pro Glu Asn Cys Ser Lys Thr Ser Lys Lys Gly Asp Leu Leu Asn Ala His Tyr Asp Gly Tyr Leu Ala Lys Asp Gly 65 <210> 1552 <211> 52 <212> PRT <213> Homo sapiens <400> 1552 Met Leu Glu Glu Leu Lys Ala Gly Gln Glu Leu Glu Gln Thr Ile Ser His Gly Phe Ala Arg Gly Val Arg Gly Val Ala Ile Val Gly 25 Lys Gly Leu Glu Trp His Gly Cys Trp Trp Met Cys His Gly Tyr Arg Ile Leu Ala Gly 50 -<210> 1553 <211> 37 <212> PRT <213> Homo sapiens <400> 1553 Met Arg Leu Gly Ser Ser Lys Leu Lys Ser Asn Gln Leu Leu Gln Glu 10 Ala Leu Ser Arg Met Lys Trp Gly Gly Pro Ser Phe Gln Pro Arg Lys 25 Pro Thr Val Pro Gly 35 <210> 1554 <211> 57 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -13..-1

<400> 1554 Met Leu Leu Leu Leu Leu Leu Pro Leu Ala Leu Gly Asp Lys Gly -10 -5 Asp Gly Gly Arg Gln Thr Ile Trp Gly Trp Leu Leu Ala Ala Ser Ala 10 Gly Ala Gly Asp Gly Ala Gly Gly Pro Val Cys Pro Cys Ala Leu Leu 20 25

30

Leu Leu Pro Pro Gly Trp Leu Asp 40

<210> 1555

<211> 95

<212> PRT

<213> Homo sapiens

<220>

<221> SIGNAL

<222> -18..-1

<400> 1555

Met Lys Leu Met Val Leu Met Leu Ala Ala Leu Leu Leu His Cys
-15 -10 -5

Tyr Ala Asp Ser Gly Cys Lys Leu Leu Glu Asp Met Val Glu Lys Thr 1 5 10

Ile Asn Ser Asp Ile Ser Ile Pro Glu Tyr Lys Glu Leu Leu Gln Glu
15 20 25 30

Phe Ile Asp Ser Asp Ala Ala Ala Glu Ala Met Gly Lys Phe Lys Gln 35 40 45

Cys Phe Leu Asn Gln Ser His Arg Thr Leu Lys Asn Phe Gly Leu Met 50 55 60

Met His Thr Val Tyr Asp Ser Ile Trp Cys Asn Met Lys Ser Asn 65 70 75

<210> 1556

<211> 95

<212> PRT

<213> Homo sapiens

<220>

<221> SIGNAL

<222> -31..-1

<400> 1556

Met Val Ala Met Ala Ala Gly Pro Ser Gly Cys Leu Val Pro Ala Phe
-30 -25 -20

Gly Leu Arg Leu Leu Leu Ala Thr Val Leu Gln Ala Val Ser Ala Phe
-15 -10 -5 1

Gly Ala Glu Phe Ser Ser Glu Ala Cys Arg Glu Leu Gly Phe Ser Ser
5 10 15

Asn Leu Cys Ser Ser Cys Asp Leu Leu Gly Gln Phe Asn Leu Leu 20 25 30

Gln Leu Asp Pro Asp Cys Arg Gly Cys Cys Gln Glu Glu Ala Gln Phe
35 40 45

Glu Thr Lys Lys Leu Tyr Ala Gly Ala Ile Leu Glu Val Cys Gly
50 55 60

<210> 1557

<211> 101

<212> PRT

<213> Homo sapiens

<220>

<221> SIGNAL

<222> -32..-1

<400> 1557

Met Phe Ala Pro Ala Val Met Arg Ala Phe Arg Lys Asn Lys Thr Leu
-30 -25 -20

Gly Tyr Gly Val Pro Met Leu Leu Leu Ile Val Gly Gly Ser Phe Gly
-15 -5

```
Leu Arg Glu Phe Ser Gln Ile Arg Tyr Asp Ala Val Lys Ser Lys Met
Asp Pro Glu Leu Glu Lys Lys Leu Lys Glu Asn Lys Ile Ser Leu Glu
Ser Glu Tyr Glu Lys Ile Lys Asp Ser Lys Phe Asp Asp Trp Lys Asn
                             40
Ile Arg Gly Pro Arg Pro Trp Glu Asp Pro Asp Leu Leu Gln Gly Lys
    50
                         55
Lys Ser Arg Lys Pro
<210> 1558
<211> 115
<212> PRT -
<213> Homo sapiens
<22.0>
<221> SIGNAL
<222> -51..-1
<400> 1558
Met Gln Ala Gln Ala Pro Val Val Val Thr Gln Pro Gly Val Gly
                        -45
Pro Gly Pro Ala Pro Gln Asn Ser Asn Trp Gln Thr Gly Met Cys Asp
                    -30
                                         -25
Cys Phe Ser Asp Cys Gly Val Cys Leu Cys Gly Thr Phe Cys Phe Pro
                -15
                                    -10
Cys Leu Gly Cys Gln Val Ala Ala Asp Met Asn Glu Cys Cys Leu Cys
Gly Thr Ser Val Ala Met Arg Thr Leu Tyr Arg Thr Arg Tyr Gly Ile
                        20
Pro Gly Ser Ile Cys Asp Asp Tyr Met Ala Thr Leu Cys Cys Pro His
                    35
                                        40
Cys Thr Leu Cys Gln Ile Lys Arg Asp Ile Asn Arg Arg Arg Ala Met
                                    55.
Arg Thr Phe
<210> 1559
<211> 126
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -24..-1
<400> 1559
Met Asp Lys Ser Leu Leu Leu Glu Leu Pro Ile Leu Leu Cys Cys Phe
                -20
                                    -15
Arg Ala Leu Ser Gly Ser Leu Ser Met Arg Asn Asp Ala Val Asn Glu
Ile Val Ala Val Lys Asn Asn Phe Pro Val Ile Glu Ile Val Arg Cys
Arg Met Cys His Leu Gln Phe Pro Gly Glu Lys Cys Ser Arg Gly Arg
                    30
                                        35
Gly Ile Cys Thr Ala Thr Thr Glu Glu Ala Cys Met Val Gly Arg Met
               45
                                    50
Phe Lys Arg Asp Gly Asn Pro Trp Leu Thr Phe Met Gly Cys Leu Lys
                                65
Asn Cys Ala Asp Val Lys Gly Ile Arg Trp Ser Val Tyr Leu Val Asn
                            80
Phe Arg Cys Xaa Arg Ser His Asp Leu Cys Asn Glu Asp Leu
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<210> 1560
 <211> 102
 <212> PRT
 <213> Homo sapiens
 <220>
 <221> SIGNAL
 <222> -16..-1
 <400> 1560
Met Asp Leu Leu Trp Ile Leu Pro Ser Leu Trp Leu Leu Leu Gly
                         -10
Gly Pro Ala Cys Leu Lys Thr Gln Glu His Pro Ser Cys Pro Gly Pro
Arg Glu Leu Glu Ala Ser Lys Val Val Leu Leu Pro Ser Cys Pro Gly
            20
                                 25
Ala Pro Gly Ser Pro Gly Glu Lys Gly Ala Pro Gly Pro Gln Gly Pro
                             40
 Pro Gly Pro Pro Gly Lys Met Gly Pro Lys Gly Glu Pro Gly Asp Pro
                         55
Val Asn Leu Leu Arg Cys Gln Glu Gly Pro Arg Asn Cys Arg Glu Leu
                    70
Leu Ser Arg Ala Pro Pro
<210> 1561
<211> 60
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -19..-1
<400> 1561
Met Glu Ser Pro Ser Xaa Ser Ala Val Val Leu Pro Ser Thr Pro Gln
                -15
                                    -10
Ala Ser Ala Asn Pro Ser Ser Pro Tyr Thr Asn Ser Ser Arg Lys Gln
                           5
Pro Met Ser Ala Thr Leu Arg Glu Arg Leu Arg Lys Thr Arg Phe Ser
                       20
Phe Asn Ser Ser Xaa Asn Val Val Asn Val Leu Lys
<210> 1562
<211> 97
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -16..-1
<400> 1562
Met Asp Phe Trp Leu Trp Pro Leu Tyr Phe Leu Pro Val Ser Gly Ala
                        -10
Leu Arg Ile Leu Pro Glu Val Lys Val Glu Gly Glu Leu Gly Gly Ser
                                   10
Val Thr Ile Lys Cys Pro Leu Pro Glu Met His Val Arg Ile Tyr Leu
                               25
Cys Arg Glu Met Ala Gly Ser Gly Thr Cys Gly Thr Val Val Ser Thr
```

WO 99/53051 657 Thr Asn Phe Ile Xaa Ala Glu Tyr Lys Gly Arg Val Thr Leu Arg Ala 55 Ile Pro Thr Gln Glu Ser Val Pro Ser Gly Gly Asn Thr Ala Asp Arg Lys <210> 1563 <211> 82 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -34..-1 <400> 1563 Met Val Gly Glu Ala Gly Arg Asp Leu Arg Arg Arg Ala Val Ala -30 -25 Val Thr Ala Glu Lys Met Ala Val Leu Ala Pro Leu Ile Ala Leu Val -15 -10 - 5 Tyr Ser Xaa Pro Arg Leu Ser Arg Trp Leu Ala Gln Pro Tyr Tyr Leu 10 Leu Ser Xaa Leu Leu Ser Xaa Ala Phe Leu Leu Val Arg Xaa Leu Pro 20 25 Pro Leu Cys His Gly Leu Pro Thr Gln Arg Glu Xaa Gly Asn Pro Ser Xaa Xaa <210> 1564 <211> 48 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -17..-1 <400> 1564 Met Ala Gln Leu Trp Leu Ser Cys Phe Leu Leu Pro Ala Leu Val Val -10 -5 Ser Val Ala Ala Asn Val Ala Pro Xaa Phe Leu Ala Asn Met Thr Ser 10 Val Ile Leu Pro Glu Asp Cys Leu Trp Val Pro Arg Pro Ser Gly Trp 20 <210> 1565 <211> 105 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -34..-1 <400> 1565 Met Val Gly Glu Ala Gly Arg Asp Leu Arg Arg Arg Ala Val Ala -30 -25 -20 Val Thr Ala Glu Lys Met Ala Val Leu Ala Pro Leu Ile Ala Leu Val -15 -10 Tyr Ser Val Pro Arg Leu Ser Arg Trp Leu Ala Gln Pro Tyr Tyr Leu

Leu Ser Ala Leu Leu Ser Ala Ala Phe Leu Leu Val Arg Lys Leu Pro

10

25

Pro Leu Cys His Gly Leu Pro Thr Gln Arg Glu Xaa Gly Asn Pro Cys
35 40 40 45

Asp Phe Asp Trp Arg Glu Val Glu Ile Leu Met Phe Leu Ser Ala Ile
50 55 60

Val Met Met Lys Asn Arg Arg Ser Ser

<210> 1566 <211> 88 <212> PRT <213> Homo sapiens

<220>
<221> SIGNAL
<222> -19..-1

<400> 1566

Met Val Ala Trp Arg Ser Ala Phe Leu Val Cys Leu Ala Phe Ser Leu
-15
-10
-5

Ala Thr Leu Val Gln Arg Gly Ser Gly Asp Phe Asp Asp Phe Asn Leu
1 5 10

Glu Asp Ala Val Lys Glu Thr Ser Ser Val Lys Gln Pro Trp Asp His
15 20 25

Thr Thr Thr Thr Thr Asn Arg Pro Gly Thr Thr Arg Ala Pro Ala 30 35 40 45 Lys Pro Pro Gly Ser Gly Leu Asp Leu Ala Asp Ala Leu Asp Asp Gln

50 55 60

Asp Asp Gly Arg Arg Asn Arg Val

<210> 1567

<211> 119

<212> PRT

<213> Homo sapiens

<220>

<221> SIGNAL

<222> -53..-1

<400> 1567

Met Ala Asp Pro Asp Pro Arg Tyr Pro Arg Ser Ser Ile Glu Asp Asp
-50
-45
-40

Phe Asn Tyr Gly Ser Ser Val Ala Ser Ala Thr Val His Ile Arg Met
-35
-25

Ala Phe Leu Arg Lys Val Tyr Ser Ile Leu Ser Leu Gln Val Leu Leu
-20 -15 -10

Thr Thr Val Thr Ser Thr Val Phe Leu Tyr Phe Glu Ser Val Arg Thr
-5 1 5 10

Phe Val His Glu Ser Pro Ala Leu Ile Leu Leu Phe Ala Leu Gly Ser

Leu Gly Leu Ile Phe Ala Leu Xaa Leu Asn Arg His Lys Tyr Pro Leu 30 35 40

Asn Leu Tyr Leu Leu Phe Gly Phe Thr Leu Leu Glu Ala Leu Thr Val 45 50 55

Ala Val Val Thr Val Leu

<210> 1568

<211> 104

<212> PRT

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<220>

<221> SIGNAL <222> -55..-1

<400> 1568

Met Ser Ser Gln Lys Gly Asn Val Ala Arg Ser Arg Pro Gln Lys His -55
-55
-50
-50
-50
-50
-50
-40
-40
Gln Asn Thr Phe Ser Phe Lys Asn Asp Lys Phe Asp Lys Ser Val Gln -35
-35
-30
-25
Thr Lys Ser Met Asn Asn Leu Ser Phe Ser Glu Leu Cys Cys Leu Phe -20
-5
Cys Cys Pro Pro Cys Pro Gly Lys Ile Ala Ser Lys Leu Ala Phe Leu -5
-5
Pro Pro Asp Pro Thr Tyr Thr Leu Met Cys Asp Glu Ser Gly Ser Val 10
Leu Tyr Ile Cys Leu Asn Glu Gln Thr Gly Ser Ile Leu Leu Glu

Lys Lys Met Leu Leu Ser Val Ser

Lys Lys Met Leu Leu Ser Val Ser 45

<210> 1569

<211> 126

<212> PRT

<213> Homo sapiens

<220>

<221> SIGNAL

<222> -62..-1

<400> 1569

Met Arg Asn Lys Lys Ile Leu Lys Glu Asp Glu Leu Leu Ser Glu Thr
-60
-55
-50

Gln Gln Ala Ala Phe His Gln Ile Ala Met Glu Pro Phe Glu Ile Asn
-45
-40
-35

Val Pro Lys Pro Lys Arg Arg Asn Gly Val Asn Phe Ser Leu Ala Val
-30
-25
-20
-15

Val Val Ile Tyr Leu Ile Leu Leu Thr Ala Gly Ala Gly Leu Leu Val

Val Gln Val Leu Asn Leu Gln Ala Arg Leu Arg Val Leu Glu Met Tyr

Phe Leu Asn Asp Thr Leu Ala Ala Glu Asp Ser Pro Ser Phe Ser Leu 20 25 30

Leu Gln Ser Ala His Pro Gly Glu His Leu Ala Gln Gly Ala Ser Arg
35 40 45

Leu Gln Ser Cys Arg Pro Asn Ser Pro Gly Ser Ala Ser Xaa

<210> 1570

<211> 134

<212> PRT

<213> Homo sapiens

<220>.

<221> SIGNAL

<222> -56..-1

<400> 1570

Met Ala Pro Thr Lys Pro Ser Phe Gln Gln Asp Pro Ser Arg Arg Glu
-55 -50 -45

Arg Leu Gln Ala Leu Arg Lys Glu Lys Ser Arg Asp Ala Ala Arg Ser
-40 -35 -30

Arg Arg Gly Lys Glu Asn Phe Glu Phe Tyr Glu Leu Ala Lys Leu Leu
-20 -15

Pro Leu Pro Ala Ala Ile Thr Ser Gln Leu Asp Lys Ala Ser Ile Ile

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660
  Arg Leu Thr Ile Ser Tyr Leu Lys Met Arg Asp Phe Ala Asn Gln Gly
                          15
                                               20
  Asp Pro Pro Trp Asn Leu Arg Met Glu Gly Pro Pro Pro Asn Thr Ser
                      30
                                           35
  Val Lys Val Ile Gly Ala Gln Arg Arg Arg Ser Pro Ser Ala Leu Ala
                                      50
  Ile Glu Val Phe Glu Ala His Leu Gly Ser His Ile Leu Gln Ser Trp
                                  65
  Met Ala Leu Tyr Leu His
         75
  <210> 1571
  <211> 28
  <212> PRT
  <213> Homo sapiens
  <220>
  <221> SIGNAL
  <222> -20..-1
  <400> 1571
  Met Glu Glu Leu Gln Asp Gln Ala Leu Leu Ser Val Cys Ser Thr Asp
                     -15
                                          -10
  Val Thr Thr Ala His Ala Trp Leu Thr Val Leu Val
                  1
  <210> 1572
  <211> 28
  <212> PRT
 <213> Homo sapiens
 <220>
 <221> SIGNAL
 <222> -20..-1
 <400> 1572
 Met Glu Glu Leu Gln Asp Gln Ala Leu Leu Ser Val Cys Ser Thr Asp
 -20
                     -15
                                          -10
 Val Thr Thr Ala His Ala Trp Leu Thr Val Leu Val
                 1
 <210> 1573
 <211> 47
 <212> PRT
. <213> Homo sapiens
 <220>
 <221> SIGNAL
 <222> -45..-1
 <400> 1573
 Met Val Gly Arg Val Arg Val Cys Arg Lys Tyr Pro Pro Thr Thr Leu
                     -40
                                         -35
 Trp Glu Gly Ala Arg Gly His Arg Gln Ile Ser Val Ser Pro Trp Asn
                 -25
                                     -20
 Ile Cys Cys Ala Ala Ala Ala Ala Ala Ala Gly Ser Arg Ile
                                 -5
 <210> 1574
 <211> 137
 <212> PRT
 <213> Homo sapiens
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<220>
 <221> SIGNAL
 <222> -52..-1
 <400> 1574
 Met Lys Arg Leu Glu Ala Lys Tyr Ala Pro Leu His Leu Val Pro Leu
         -50
                              -45
 Ile Glu Arg Leu Gly Thr Pro Gln Gln Ile Ala Ile Ala Arg Glu Gly
     -35
                         -30
 Asp Leu Leu Thr Lys Glu Arg Leu Cys Cys Gly Leu Ser Met Phe Glu
                     -15
                                          -10
 Val Ile Leu Thr Arg Ile Arg Ser Tyr Leu Gln Asp Pro Ile Trp Arg
 Gly Pro Pro Pro Thr Asn Gly Val Met His Val Asp Glu Cys Val Glu
                             20
 Phe His Arg Leu Trp Ser Ala Met Gln Phe Val Tyr Cys Ile Pro Val
                         35
 Gly Thr Asn Glu Phe Thr Ala Glu Gln Cys Phe Gly Asp Gly Leu Asn
 Trp Ala Gly Ser Pro Xaa Leu Ser Cys Xaa Ala Ser Ser Val Ala Leu
                 65
 Thr Cys Ser Thr Ser Val Thr Thr Cys
 <210> 1575
 <211> 101
 <212> PRT
 <213> Homo sapiens
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 <221> SIGNAL
<222> -71..-1
 <400> 1575
Met Ala Leu Val Pro Cys Gln Val Leu Arg Met Ala Ile Leu Leu Ser
   -70
                         -65
                                             -60
Tyr Cys Ser Ile Leu Cys Asn Tyr Lys Ala Ile Glu Met Pro Ser His
                     -50
                                         -45
Gln Thr Tyr Gly Gly Ser Trp Lys Phe Leu Thr Phe Ile Asp Leu Val
                 -35
                                     -30
                                                         -25
Ile Gln Ala Val Phe Phe Gly Ile Cys Val Leu Xaa Asp Leu Ser Ser
          -20
                                 -15
Leu Leu Thr Arg Gly Ser Gly Asn Gln Glu Gln Glu Arg Gln Leu Lys
Lys Leu Ile Ser Leu Arg Asp Trp Met Leu Ala Val Leu Ala Phe Leu
                                                             25
Leu Gly Phe Leu Leu
                30
<210> 1576
<211> 79
<212> PRT
<213> Homo sapiens
<220>
<221> SIGNAL
<222> -69..-1
<400> 1576
Met Ala Thr His His Leu Gly Leu Pro Ala Ser Gln Pro Leu Pro Gly
                -65
                                    -60
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Ile Leu Ser Arg Ala Pro Ser Leu Pro Pro Arg Ser Pro Ala Thr Arg

662 -50 . -45 Ser Arg Val Ser Ser Pro Trp Gly Glu Ser Ser Ser Leu Leu Phe -30 -25 Pro Asp Cys His Ile Ser Phe Pro Ala Leu Thr Gly Ser Gln Leu Leu -15 -10 Gly Asp Thr Ile Pro Arg Pro His Leu Pro Pro Thr Ala Ala Cys 5 <210> 1577 <211> 108 <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -35..-1 <400> 1577 Met Thr Pro Ser Arg Leu Pro Trp Leu Leu Ser Trp Val Ser Ala Thr -30 -25 Ala Trp Arg Ala Ala Arg Ser Pro Leu Leu Cys His Ser Leu Arg Lys -15 -10 Thr Ser Ser Ser Gln Gly Gly Lys Ser Glu Leu Val Lys Gln Ser Leu 5 10 Lys Lys Pro Lys Leu Pro Glu Gly Arg Phe Asp Ala Pro Glu Asp Ser 20 His Leu Glu Lys Glu Pro Leu Glu Lys Phe Pro Asp Asp Val Xaa Pro 40 Val Thr Lys Glu Lys Gly Gly Pro Arg Gly Pro Glu Pro Thr Arg Tyr 50 55 Gly Asp Trp Glu Arg Lys Gly Arg Cys Ile Asp Phe <210> 1578 <211> 81. <212> PRT <213> Homo sapiens <220> <221> SIGNAL <222> -51..-1 <400> 1578 Met Glu Lys Leu Arg Arg Val Leu Ser Gly Gln Asp Asp Glu Glu Gln -50 -45 -40 Gly Leu Thr Ala Gln Val Leu Asp Ala Ser Ser Leu Ser Phe Asn Thr -30 -25 Arg Leu Lys Trp Phe Ala Ile Cys Phe Val Cys Gly Val Phe Phe Ser -15 -10 Ile Leu Gly Thr Gly Leu Leu Trp Leu Pro Gly Gly Ile Lys Leu Phe Ala Val Phe Tyr Thr Leu Gly Asn Leu Ala Ala Leu Xaa Val His Ala 20 Xaa 30 <210> 1579 <211> 108 <212> PRT <213> Homo sapiens <220> <221> SIGNAL

<222> -93..-1

<400> 1579

Met Cys Glu Asn Gln Glu Glu Pro Ala Gly Ser Val Cys Cys His Arg
-90 -85 -80

Val Ser Ala Cys Arg Gly Gly Thr Pro Gly Gly Gly Arg Gly Gln Ser
-75 -70 -65

His Cys Arg Gly Pro Asp Trp Glu Asn Asn Asp Met Ala Gly Ala Ser
-60 -50

Leu Gly Ala Arg Phe Tyr Arg Gln Ile Lys Arg His Pro Gly Ile Ile
-45 -35 -30

Pro Met Ile Gly Leu Ile Cys Leu Gly Met Gly Ser Ala Ala Leu Tyr
-25
-20
-15

Leu Leu Arg Leu Ala Leu Arg Ser Pro Asp Val Trp Leu Gly Gln Lys
-10 -5 1

Glu Gln Pro Gly Ala Leu Glu Pro Pro Glu Pro Gln 5 . 10 15

<210> 1580

<211> 134

<212> PRT

<213> Homo sapiens

<220>

<221> SIGNAL

<222> -16..-1

<400> 1580

Met Ala Ala Ala Gly Leu Ala Leu Leu Xaa Arg Arg Val Ser Ser Ala
-15 -5

Leu Lys Ser Ser Arg Ser Leu Ile Thr Pro Gln Val Pro Ala Cys Thr
1 5 10 15

Gly Phe Phe Leu Ser Leu Leu Pro Lys Ser Thr Pro Asn Val Thr Ser 20 25 30

Phe His Gln Tyr Arg Leu Leu His Thr Thr Leu Ser Arg Lys Gly Leu 35 40 45

Glu Glu Phe Phe Asp Asp Pro Lys Asn Trp Gly Gln Glu Lys Val Lys 50 55 60

Ser Gly Ala Ala Trp Thr Cys Gln Gln Leu Arg Asn Lys Ser Asn Glu 65 70 75 80

Asp Leu His Lys Leu Trp Tyr Val Leu Leu Lys Glu Arg Asn Met Leu 85 90 95

Leu Thr Leu Glu Glu Glu Ala Lys Arg Gln Arg Leu Pro Met Pro Ser 100 105 110

Pro Glu Arg Leu Asp Arg

11:

<210> 1581

<211> 64

<212> PRT

<213> Homo sapiens

<400> 1581

Met Asn Glu Ser Lys Pro Gly Asp Ser Gln Asn Leu Ala Cys Val Phe 1 5 10 15

Cys Arg Lys His Asp Asp Cys Pro Asn Lys Tyr Gly Glu Lys Lys Thr

Lys Glu Lys Trp Asn Leu Thr Val His Tyr Tyr Cys Leu Leu Met Ser

Ser Gly Ile Trp Gln Arg Gly Lys Glu Glu Glu Gly Val Met Val Phe
50 55 60

<210> 1582

<211> 79

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664
 <212> PRT
 <213> Homo sapiens
<400> 1582
Met Ala Val Ala Arg Ala Gly Val Leu Gly Val Gln Trp Leu Gln Arg
Ala Ser Arg Asn Val Met Pro Leu Gly Ala Arg Thr Ala Ser His Met
Thr Lys Asp Met Phe Pro Gly Pro Tyr Pro Arg Thr Pro Glu Glu Arg
Ala Ala Ala Lys Lys Tyr Asn Met Arg Val Glu Asp Tyr Glu Pro
                         55
Tyr Pro Asp Asp Gly Met Gly Tyr Gly Asp Leu Phe Leu Xaa Val
<210> 1583
<211> 66
<212> PRT
<213> Homo sapiens
<400> 1583
Met Glu Val Asp Ala Pro Gly Val Asp Gly Arg Asp Gly Leu Arg Glu
Arg Arg Gly Phe Ser Glu Gly Gly Arg Gln Asn Phe Asp Val Arg Pro
Gln Ser Gly Ala Asn Gly Leu Pro Lys His Ser Tyr Trp Leu Asp Leu
Trp Leu Phe Ile Leu Phe Asp Val Val Phe Leu Phe Val Tyr Phe
   50
Leu Pro
65
<210> 1584
<211> 45
<212> PRT
<213> Homo sapiens
<400> 1584
Met Tyr Val Tyr Val Cys Val Trp Val Cys Val Tyr Thr Val Glu Ser
Lys Leu Glu Asn Ser Ser Ile Tyr Pro Pro Pro Ser Pro Val Glu Xaa
                                25
Lys Lys Ile Phe Thr Phe Val Thr Phe Leu Phe Pro Pro
<210> 1585
<211> 25
<212> PRT
<213> Homo sapiens
<400> 1585
Met Gly Pro Gly Gly Ala Leu His Gly Gly Met Lys Thr Leu Leu Pro
Trp Thr Ala Arg Ala Ser Arg Ser Pro
<210> 1586
<211> 98
<212> PRT
<213> Homo sapiens
<400> 1586
Met Tyr Gly Lys Gly Lys Ser Asn Ser Ser Ala Val Pro Ser Asp Ser
Gln Ala Arg Glu Lys Leu Ala Leu Tyr Val Tyr Glu Tyr Leu Leu His
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20 25 30 Val Gly Ala Gln Lys Ser Ala Gln Thr Phe Leu Ser Glu Ile Arg Trp

35

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Glu Lys Asn Ile Thr Leu Gly Glu Pro Pro Gly Phe Leu His Ser Trp
                         55
 Trp Cys Val Phe Trp Asp Leu Tyr Cys Ala Ala Pro Glu Arg Arg Glu
                     70
 Thr Cys Glu His Ser Ser Glu Ala Lys Ala Phe His Asp Tyr Val Xaa
 Asn Ile
 <210> 1587
 <211> 50
 <212> PRT
 <213> Homo sapiens
 <400> 1587
 Met Cys Leu Leu Glu Val Pro Gly Ala Thr Lys Leu Leu Ala Ala Arg
 Arg Thr Leu Lys Arg Asn Gly Ile Ser Pro Pro Asn Gln Glu Gly Leu
Ala Leu Leu Gly Glu Leu Thr Thr His Lys Gln Met Arg Thr Lys
 Thr Glu
    50
<210> 1588
 <211> 32
<212> PRT
<213> Homo sapiens
<400> 1588
Met Asn Arg Thr Ala Met Arg Ala Ser Gln Lys Asp Phe Glu Asn Ser
Xaa Asn Gln Val Lys Leu Leu Lys Lys Asp Pro Gly Asn Glu Xaa Ser
<210> 1589
<211> 58
<212> PRT
<213> Homo sapiens
<400> 1589
Met Ala Ser Ser Gly Ala Gly Asp Pro Leu Asp Ser Lys Arg Gly Glu
Ala Pro Phe Ala Gln Arg Ile Asp Pro Thr Arg Glu Lys Leu Thr Pro
Glu Gln Leu His Ser Met Arg Gln Ala Glu Leu Pro Ser Gly Arg Arg
Ser Tyr His Gly Gly Glu Pro Gly Thr Ser
    50
<210> 1590
<211> 98
<212> PRT
<213> Homo sapiens
<400> 1590
Met Ser Ser Asp Asp Lys Ser Lys Ser Asn Asp Pro Lys Thr Glu Pro
Lys Asn Cys Asp Pro Lys Cys Glu Gln Lys Cys Glu Ser Lys Cys Gln
                                25
Pro Ser Cys Leu Lys Lys Leu Leu Gln Arg Cys Phe Glu Lys Cys Pro
Trp Glu Lys Cys Pro Ala Pro Pro Lys Cys Leu Pro Cys Pro Ser Gln
Ser Pro Ser Ser Cys Pro Pro Gln Pro Cys Thr Lys Pro Cys Pro Pro
                   70
Lys Cys Pro Ser Ser Cys Pro His Ala Cys Pro Xaa Pro Cys Pro Pro
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Pro Glu

<210> 1591

<211> 43

<212> PRT

<213> Homo sapiens

<400> 1591

Met Cys Gly Gly Trp Asp Pro Val Ala His Pro Cys Arg Ser Cys Pro 1 5 10 15

Ser His Ala Arg Arg Arg Val Phe Val Val Thr Pro Cys Cys His Leu 20 25 30

Phe Ser Ser Leu Cys Glu Asp Leu Asp Trp Gln

<210> 1592

<211> 157

<212> PRT

<213> Homo sapiens

<400> 1592

Met Ala Thr Pro Pro Lys Arg Arg Ala Val Glu Ala Thr Gly Glu Lys

1 5 10 15

Val Leu Arg Tyr Glu Thr Phe Ile Ser Asp Val Leu Gln Arg Asp Leu
20 25 30

Arg Lys Val Leu Asp His Arg Asp Lys Val Tyr Glu Gln Leu Ala Lys
35 40 45

Tyr Leu Gln Leu Arg Asn Val Ile Glu Arg Leu Gln Glu Ala Lys His
50 55 60

Ser Glu Leu Tyr Met Gln Val Asp Leu Gly Cys Asn Phe Phe Val Asp 65 70 75 80

Thr Val Val Pro Asp Thr Ser Arg Ile Tyr Val Ala Leu Gly Tyr Gly
85 90 95

Phe Phe Leu Glu Leu Thr Leu Ala Glu Ala Leu Lys Phe Ile Asp Arg 100 105 110

Lys Ser Ser Leu Leu Thr Glu Leu Ser Asn Ser Leu Thr Lys Asp Ser 115 120 125

Met Asn Ile Lys Ala His Ile His Met Leu Leu Glu Gly Leu Arg Glu
130 135 140

Leu Gln Gly Leu Gln Asn Phe Pro Glu Lys Pro His His 145 150 155

<210> 1593

<211> 119

<212> PRT

<213> Homo sapiens

<400> 1593

Met Glu Ala Ser Ala Leu Thr Ser Ser Ala Val Thr Ser Val Ala Lys

1 10 15

Val Val Arg Val Ala Ser Gly Ser Ala Val Val Leu Pro Leu Ala Arg
20 .25 30

Ile Ala Thr Val Val Ile Gly Gly Val Val Ala Val Pro Met Val Leu 35 40 45

Ser Ala Met Gly Phe Thr Ala Ala Gly Ile Ala Ser Ser Ile Ala

Ala Lys Met Met Ser Ala Ala Ile Ala Asn Gly Gly Val Ala 65 70 75 80

Ser Gly Ser Leu Val Ala Thr Leu Gln Ser Leu Gly Ala Thr Gly Leu

85 90 95
Ser Gly Leu Thr Lys Xaa Ile Leu Gly Ser Ile Gly Ser Ala Ile Ala
100 105 110

Ala Val Ile Ala Arg Phe Tyr

<211> 81 <212> PRT <213> Homo sapiens <400> 1594 Met Tyr Ile Gln Cys Cys Glu Trp Leu Gln Ser Trp Arg Ser Lys Asp Glu Phe Cys Leu Glu Glu Ser Gly Lys Ala Ser Trp Arg Arg Glu Gln Trp His Gly Pro Xaa Xaa Val Arg Ser Phe Gln Phe Ile Pro Phe Lys 35 40 His Cys Ser His Val Ala Phe Lys His Ser Ile Val Leu Ala Val Thr 55 Gln Ala His Ser Ala Lys Gly Ser Thr Ser Phe Ser Ala Met Arg Thr 70 Tyr <210> 1595 <211> 65 <212> PRT <213> Homo sapiens <400> 1595 Met Val Gly Val Ser Val Cys His His Ile Arg Val Gly Ile Lys Arg Arg Lys Ala Ala Leu Leu Glu Leu Cys Gly Leu Leu Gln Val Arg Val 20 25 Ala Gly Asn Arg Thr Thr Leu Leu Leu Glu Glu Lys Arg Asn Ser Phe 40 . Ser Ala Xaa Thr Arg Lys Ala Val Phe Phe Ser Gly Asp Leu His Phe 55 Ser 65 <210> 1596 <211> 111 <212> PRT <213> Homo sapiens <400> 1596 Met Pro Ser Arg Thr Ala Arg Tyr Ala Arg Tyr Ser Pro Arg Gln Arg Arg Arg Arg Met Leu Ala Asp Arg Ser Val Arg Phe Pro Asn Asp Val 20 Leu Phe Leu Asp His Ile Arg Gln Gly Asp Leu Glu Gln Val Gly Arg Phe Ile Arg Thr Arg Lys Val Ser Leu Ala Thr Ile His Pro Ser Gly 55 Leu Ala Ala Leu His Glu Ala Val Leu Ser Gly Asn Leu Glu Cys Val Lys Leu Leu Val Lys Tyr Gly Ala Asp Ile His Gln Arg Asp Glu Ala 90 Gly Trp Thr Pro Leu His Ile Ala Cys Ser Asp Gly Tyr Leu Thr 105 <210> 1597 <211> 33 <212> PRT <213> Homo sapiens <400> 1597 Met Ala Trp Gly Gly Trp Gly Ala His Ser Ala Cys Ser Glu Glu Arg

Ala Thr Arg Pro Val Glu Gly Ala Tyr Ser Gly Arg Trp Gly Gln Ala
20 25 30

Gln

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668
 <210> 1598
 <211> 113
 <212> PRT
 <213> Homo sapiens
 <400> 1598
Met Asp Pro Asn Pro Arg Ala Ala Leu Glu Arg Gln Gln Leu Arg Leu
Arg Glu Arg Gln Lys Phe Phe Glu Asp Ile Leu Gln Pro Glu Thr Glu
             20
Phe Val Phe Pro Leu Ser His Leu His Leu Glu Ser Gln Arg Pro Pro
Ile Gly Ser Ile Ser Ser Met Glu Val Asn Val Asp Thr Leu Glu Gln
Val Glu Leu Ile Asp Leu Gly Asp Pro Asp Ala Ala Asp Val Phe Leu
                                         75
Pro Cys Glu Asp Pro Pro Pro Thr Pro Gln Ser Ser Gly Val Asp Asn
                                      90
His Leu Glu Glu Leu Ser Leu Pro Xaa Ala Tyr Ile Arg Gln Asp His
            100
                                 105
Ile
<210> 1599
<211> 58
<212> PRT
<213> Homo sapiens
<400> 1599
Met Val Val Phe Gly Tyr Glu Ala Gly Thr Lys Pro Arg Asp Ser Gly
                                     10
Val Val Pro Val Gly Thr Glu Glu Ala Pro Lys Asp Thr Lys Tyr Ile
                                 25
Ser Asn Gly Asp Ile Trp Asn Asn Ser Trp Phe Leu Trp Asn Ile Leu
Lys Leu Pro Val Gln Thr Leu Leu Gln Gly
    50
<210> 1600.
<211> 247
<212> DNA
<213> Homo sapiens
<400> 1600
gaaaattact ttgacctttt gttagtgatc ccattcagct agtaccaagc tgaagattga
                                                                       60
tattcgttaa tggttaatat aaatttactg ctctaggtta agcctaacat atgtaattgc
                                                                       120
tactageeta ttaettttta gteeattggg aateaetaaa aaaagtagag getttagett
                                                                       180
catteetegg etgettaaat catattgtaa tgttttaaat tgttatgteg teetgtataa .
                                                                       240
ccttagg
                                                                       247
<210> 1601
<211> 225
<212> DNA
<213> Homo sapiens
<400> 1601
aaaattattt tgagacaaaa catgggaaag gagggagttg gccaggagtt tatcatgaag
                                                                       60
catatacagg agtcatcccc tacgttgaca ctggtaagtt gacttcagtc acatgaaaca
                                                                       120
tgtcaccttt ccataaatac tccattccct tttgtgattt tgttctttgc acatgttgtt
                                                                      180
ctatetetge etggaatgtg ttetecacet tttgattgte tgeca
                                                                       225
<210> 1602
<211> 258
<212> DNA
<213> Homo sapiens
<400> 1602
gtgaccacag tctgcagagg ccagagagag caggaaagga aatggaaagg aacctcacct
tcatgcttgg ggaaaaggag aaacctgtgt taatgtgtct tcccaacatc ccactctctt
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<220>

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<221> misc_feature
 <222> 323
 <223> n=a, g, c or t
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                                                                         60
 caggacaaac acaaagaact ctctgcacag ttcattactc cattaggtgg ttcagatgca
                                                                        120
 attecagece ttagteaggt tetttecagt gteetcaaac acagtaagga gagtgeteta
                                                                        180
agtgactctt tgtgtctcac acaatctctt gggttcccag gtcactggtg tagtagccag
                                                                        240
 ctgcatccaa gaagccaggt gagcctgtgc caccaatcac agatactcct taccaaccat
                                                                        300
 ctgccaaccc atgccagccc tgntgcccat ggatgtgcgg ctgtccatgt gccacgccca
                                                                        360
                                                                        361
 <210> 1608
 <211> 305
 <212> DNA
 <213> Homo sapiens
<400> 1608
aagacggaag ctcggttgat gtttctgcag aagttttccc ccttggtcgg tggcggastg
                                                                         60
ctgagcgcga tagtagcagc tccggcggca gcaacattga ctacgaggaa tggcggcggc
                                                                       120
tgccgcagga cctgcagcat cccagaggtg cagattttaa tttcagtgac tgaattaaaa
                                                                       180
ggtgtcaaga agctcgaatg gtatgtaggt ctcccatggt atttcaattt aaaaagaagt
                                                                       240
aagcacttga aattttttgg tttaagcaaa tttgttttta cctttataat ttattttaaa
                                                                       300
taata
                                                                       305
<210> 1609
<211> 242
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> 152
<223> n=a, g, c or t
<400> 1609
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                                                                        60
tagaggcatt aaaggtcaga gttctgagac ctgctctgga gtgggcagtg tcaaaccggg
                                                                       120
aaatgettat ageteaaaca geteettgga anttaageta cacagaetgt attttattag
                                                                       180
cttgttaatg ggtggaacca caaatcagcg agaggcatta caatatgcta aaaattttca
                                                                       240
                                                                       242
<210> 1610
<211> 196
<212> DNA
<213> Homo sapiens
<400> 1610
ggaagcgatt tcatagccac ggtttttggc tttcatcgct ttttctacat gtttttagcc
                                                                        60
tcaccagaag tctttcatct cggtggtcca actcaggatc tcagcctcat tattttctta
                                                                       120
cccttctgga gtgcatatgt gcctttacag ttctgtttgc aaacgctgtc tagcatacta
                                                                       180
agaggatgtt agcaaa
                                                                       196
<210> 1611
<211> 228
<212> DNA
<213> Homo sapiens
<400> 1611
atattgaata agcgacccgg cctcctaggg ggtcgtcgtg gtgcagacag tttagcagaa
                                                                       60
cagcctccgc ggctccgggg agaaggtgag gtcttgtatg gatgggaagg gtgaggtgcg
                                                                      120
teggecagag gettatttat tgaegggaet gttteetttg geccaegega egtagettet
                                                                      180
gttgtccttg actgggcgcc gcctcccgcc ccgccgcctc ggaagccc
                                                                      228
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<210> 1612
 <211> 221
 <212> DNA
 <213> Homo sapiens
<220>
<221> misc_feature
 <222> 108
 <223> n=a, g, c or t
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                                                                         60
gaggagccct agaaagaaat tcaggtctcc tatgtactga tcacagcnca gaaccccagg
                                                                        120
aagccagagg tgttccaccc caatccttca ccctcacccc acatcatggt ggcccctggg
                                                                       180
acctggatgg aaaacctctg gcwtcctggg gttctgggct g
                                                                       221
<210> 1613
<211> 360
<212> DNA
<213> Homo sapiens
<400> 1613
agttgcctgc agagcctgag gtcagggaag gtctcagatg gttcatacct tggtgtatac
                                                                        60
atgagttcat aggcctggga ttaaggatta tccctgcaat cttgcctgcc ttgcagataa
                                                                       120
gctactttct gaatcctaaa gcgctcttcc agctttcaca tttgattccg tggcagaagg
                                                                       180
ctcacagcct cacaaagtgg agacaggcag acagtcccac ctcatttcaa ctccagagtt
                                                                       240
ggggaacgtg ctgggggtgc tcagccagag cetetcagec aggcettgtg aggcagaggg
                                                                       300
atcettacca ggcagatggt etggaggaga ggcagacegg gagaaagcat agtgtgecag
                                                                       360
<210> 1614
<211> 171
<212> DNA
<213> Homo sapiens
<400> 1614
cagtaaggta gcaggattca aattatttt tccagtattg acatttagaa tgtcatgttg
                                                                        60
gacatttaaa atttttctgg ttgtagcctc attactgtat agaaatcaac taccagatga
                                                                       120
gtagttgaca gacacagcta gcttggttgc ttgcttgctg ttcttgccgc c
                                                                       171
<210> 1615
<211> 193
<212> DNA
<213> Homo sapiens
<400> 1615
acatetttag tagagaeggg caateeacce geeteggete ceagagtaet gggatgaeag
                                                                        60
gcgtgagcac cacgtccggc cacaaaagag ctttgatgca cacggtgaca gccacatggt
                                                                       120
gcacceggaa gaacaagggg cetgaagtta gttagaccet cettgetggt tetaccacag
                                                                       180
tcgcacgccc cac
                                                                       193
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<211> 349
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<221> misc_feature
<222> 99
<223> n=a, g, c or t
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                                                                       60
catattgtcc aagctattcg catggaagct accagagtnc gtgaagaatg ggaacatgct
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<211> 400 <212> DNA <213> Homo sapiens <220> <221> misc_feature <222> 43

<223> n=a, g, c or t

#### <400> 1622

	(100) 1022						
	agggagggac	agagagcgaa	ctgtcagatc	ggagcgagag	cgngcgcccg	agagaggag	60 [.]
•	agagagagag	ggagggagag	gaaaagtgag	agagggaaag	agagcgcgaa	cgagggcgca	120
	gagcgagctc	ctgctgcaac	tctgctccag	cacggccagc	gccagcgccc	gccgtcggtg	180
	cactctacga	gccgtgcagc	gtgcccactg	gagttgttgt	gtatcaagga	tcgatcccct	240
	atatgcacac	acacacctcc	acctccacca	atgcactctt	cttcctcctc	cttctccaga	300
	caactgctgg	gaaaaaaata	aaacaccaac	cccaaccgtc	agcaacaagg	taasmgagcg	360
	attcgacatc	atttttttc	ctgttcaatt	ttttccttgt			400

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- (74) Agents: MARTIN, Jean-Jacques et al.; Cabinet Regimbeau, 26, avenue Kléber, F-75116 Paris (FR).

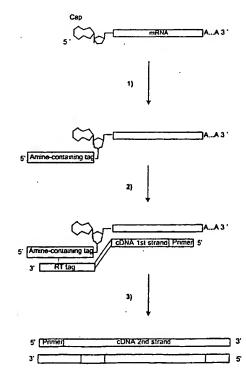
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#### (54) Title: 5' ESTS AND ENCODED HUMAN PROTEINS

#### (57) Abstract

The sequences of 5' ESTs derived from mRNAs encoding secreted proteins are disclosed. The 5' ESTs may be to obtain cDNAs and genomic DNAs corresponding to the 5' ESTs. The 5' ESTs may also be used in diagnostic, forensic, gene therapy, and chromosome mapping procedures. Upstream regulatory sequences may also be otained using the 5' ESTs. The 5' ESTs may also be used to design expression vectors and secretion vectors.



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a. CLASSIFICATION OF SUBJECT MATTER IPC 6 C12N15/11 C12N IPC 6 C12N15/10 CO7K14/47 C12P21/00 C12Q1/68 G06F17/50 C07K16/18 G06F17/30 According to International Patent Classification (IPC) or to both national classification and IPC B. FIELDS SEARCHED Minimum documentation searched (classification system followed by classification symbols) IPC 6 C12N C07K Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched Electronic data base consulted during the international search (name of data base and, where practical, search terms used) C. DOCUMENTS CONSIDERED TO BE RELEVANT Citation of document, with indication, where appropriate, of the relevant passages Relevant to claim No. BRENNER ET AL.: "Homo sapiens Xq28 χ 1.2 genomic DNA in the region of the L1CAM EMBL SEQUENCE DATABASE, 9 May 1996 (1996-05-09), XP002121588 HEIDELBERG DE Y Ac U52112 4-21 the whole document & BRENNER ET AL.: "Genomic organization of two novel genes on human Xq28: compact head to head arrangement of IDH gamma and TRAP delta is conserved in rat and mouse" GENOMICS. vol. 44, no. 1, 1997, pages 8-14, Patent family members are fisted in annex. Further documents are listed in the continuation of box C. Special categories of cited documents : T later document published after the international filing date or priority date and not in conflict with the application but "A" document defining the general state of the art which is not cited to understand the principle or theory underlying the considered to be of particular relevance invention "E" earlier document but published on or after the international "X" document of particular relevance; the claimed invention filing date cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another "Y" document of particular relevance; the claimed invention citation or other special reason (as specified) cannot be considered to involve an inventive step when the "O" document referring to an oral disclosure, use, exhibition or document is combined with one or more other such doc ments, such combination being obvious to a person skilled other means *P* document published prior to the international filing date but later than the priority date claimed *&* document member of the same patent family Date of the actual completion of the international search Date of mailing of the international search report 2 8. JAN. 2000 4 November 1999 Name and mailing address of the ISA Authorized officer European Patent Office, P.B. 5818 Patentiaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo ni, CEDER O. Fax: (+31-70) 340-3016

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Interr. nal Application No
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C.(Continua	ation) DOCUMENTS CONSIDERED TO BE RELEVANT	·
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Y .	WO 96 34981 A (GENSET ; MERENKOVA IRENA NICOLAEVNA (FR); DUMAS MILNE EDWARDS JEAN) 7 November 1996 (1996-11-07) cited in the application page 13, line 24 -page 14, line 14; claim 26	4
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Y	KATO S ET AL: "Construction of a human full-length cDNA bank" GENE, vol. 150, 1 January 1994 (1994-01-01), pages 243-250, XP002081364 ISSN: 0378-1119 cited in the application abstract page 245, left-hand column -/	6,10

Intern. nal Application No PCT/IB 99/00712

		PC1/18 99/00/12
C.(Continu	ation) DOCUMENTS CONSIDERED TO BE RELEVANT	
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y A	WO 97 38003 A (HUMAN GENOME SCIENCES INC; LI HAODONG (US); WEI YING FEI (US)) 16 October 1997 (1997-10-16) seq Id No 2 claims 10-12	7,11,20, 21 3
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Υ	WO 98 07830 A (INST GENOMIC RESEARCH ;UNIV PENNSYLVANIA (US); UNIV JOHNS HOPKINS) 26 February 1998 (1998-02-26) page 3, line 4 - line 28 page 31, line 6 -page 35, line 16	7,11-21
X	MUZNY ET AL.: "Homo sapiens, working draft sequence, 97 unordered pieces" EMBL SEQUENCE DATABASE, 3 February 1998 (1998-02-03), XP002121591 HEIDELBERG DE Ac AC004085 the whole document	1,2
<b>X</b>	ADAMS ET AL.: "EST177394 Jurkat T-cells VI homo sapiens cDNA 5' end similar to protein kinase C substrate 80K-H" EMBL SEQUENCE DATABASE, 18 April 1997 (1997-04-18), XP002121592 HEIDELBERG DE Ac AA306438 the whole document -& ADAMS ET AL.: "Initial assessment of	3
	human gene diversity and expression patterns based upon 83 million nucleotides of cDNA sequences" NATURE, vol. 377, 1995, pages 3-174, XP002069461	
A	"zr94d07.r1 NCI_CGAP_GCB1 Homo sapiens cDNA clone IMAGE:683341 5' EST" EMBL SEQUENCE DATABASE, 5 February 1997 (1997-02-05), XP002121593 HEIDELBERG DE Ac AA215334 the whole document	1,2
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C.(Continual Category *	Citation of document, with indication, where appropriate, of the relevant passages  ADAMS M D ET AL: "RAPID CDNA SEQUENCING (EXPRESSED SEQUENCE TAGS) FROM A DIRECTIONALLY CLONED HUMAN INFANT BRAIN CDNA LIBRARY" NATURE GENETICS, vol. 4, no. 4, 1 August 1993 (1993-08-01), pages 373-380, STANDARD, XP002064427 ISSN: 1061-4036		Relevant to claim No.
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A	(EXPRESSED SEQUENCE TAGS) FROM A DIRECTIONALLY CLONED HUMAN INFANT BRAIN CDNA LIBRARY" NATURE GENETICS, vol. 4, no. 4, 1 August 1993 (1993-08-01), pages 373-380, STANDARD, XP002064427		1
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International application No. PCT/IB 99/00712

### INTERNATIONAL SEARCH REPORT

Box I	Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)
This Inte	emational Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:
1. χ	Claims Nos.: - because they relate to subject matter not required to be searched by this Authority, namely:
· · ·	Rule 39.1(v) PCT - Presentation of information Although claim 12 could be considered as a mere presentation of information, Rule 39.1(v) PCT, the search has been carried out as far as possible in our systematic documentation.
2.	Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3	Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).
Box (I	Observations where unity of invention is lacking (Continuation of item 2 of first sheet)
This Inte	ernational Searching Authority found multiple inventions in this international application, as follows:
1.	As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2.	As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3.	As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
	,
4. X	No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
	Invention 1: 1-21 partially
Remark	on Protest The additional search fees were accompanied by the applicant's protest.
	No protest accompanied the payment of additional search fees.
	•

### FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.1

Although claim 12 could be considered as a mere presentation of information, Rule 39.1(v) PCT, the search has been carried out as far as possible in our systematic documentation.

Continuation of Box I.1

Rule 39.1(v) PCT - Presentation of information

### FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

1. Claims: Invention 1: 1-21 all partially

Nucleic acid comprising a sequence as in Seq.ID.No. 24, complementary sequence and fragments thereof. Polypeptide, Seq.Id.No. 812, encoded by said nucleotide sequence. Vector comprising Seq.Id.No. 24 and host cell comprising the vector. Methods of making cDNA and polypeptide utilising Seq.Id.No. 24. Array of ESTs comprising Seq.Id.No. 24, or a fragment thereof. An antibody binding to an epitop of the polypeptide of Seq.Id.No. 812. A computer readable medium and a computer system storing and/or utilising the sequence of Seq.Id.No. 24 or 812.

2. Claims: Invention 2-811 : 1-21 all partially

Idem as subject 1 but limited to each of the DNA sequences as in Seq.Id.No. 25-811 and 1600-1622, and corresponding polypeptides when applicible, where invention 2 is limited to Seq.Id.No. 25 and 813, invention 3 is limited to Seq.Id.No. 26 and 814, ....., invention 788 is limited to Seq.Id.No. 811 and 1599, invention 789 is limited to Seq.Id.No. 1600, invention 790 is limited to Seq.Id.No. 1601, ...., invention 811 is limited to Seq.Id.No. 1622.

Information on patent family members

International Application No
PCT/IB 99/00712

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